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18jul02 15:16:43 User219783 Session D1851.2

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File 158:DIOGENES(R) 1976-2002/Jul W2

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Set Items Description

Set	Items	Description
S1	499	((INTERLEUKIN OR IL)(W)(1 OR 1A OR 1B OR 1ALPHA OR 1BETA OR 1A OR 1B OR 1ALPHA OR 1BETA OR 1RN OR 1RN) OR IL1 OR IL1A? OR IL1A? OR IL1B? OR IL1B? OR IL1RN OR IL1RN) AND (MENOPAUS? OR PERIMENOPAUS? OR PREMENOPAUS? OR CHANGE(1W)LIFE)
S2	53	S1 AND (MUTAGEN? OR MUTAT? OR MUTANT? ? OR POLYMORPH? OR POLY(W)(MORPHISM? ? OR MORPHIC?) OR (VARIAT? OR VARIANT? ?)(5N-ALLEN?)
S3	50	RD (unique items)

>>>No matching display code(s) found in file(s): 65, 129, 158, 624

3/3,AB/1 (Item 1 from file: 149)

DIALOG(R)File 149:TGG Health&Wellness DB(SM)

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-key terms

Searcher : Shears 308-4994

09/632657

02085035 SUPPLIER NUMBER: 87347833 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Announcing the American Diabetes Association's 62nd scientific sessions.
Diabetes, 51, 6, NA(68)
June,
2002
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0012-1797
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 15380 LINE COUNT: 03398

3/3,AB/2 (Item 2 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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02079894 SUPPLIER NUMBER: 86035147 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Familial expansile osteolysis (excessive RANK effect) in a 5-generation
American kindred.
Whyte, Michael P.; Reinus, William R.; Podgornik, Michelle N.; Mills,
Barbara G.
Medicine, 81, 2, 101(21)
March,
2002
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0025-7974
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 14115 LINE COUNT: 01149

3/3,AB/3 (Item 3 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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02072288 SUPPLIER NUMBER: 84666748 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Interaction of hemostatic genetics with hormone therapy *; new insights to
explain arterial thrombosis in postmenopausal women.
Braunstein, Joel B.; Kershner, Dawn Warner; Bray, Paul; Gerstenblith, Gary;
Schulman, Steven P.; Post, Wendy S.; Blumenthal, Roger S.
Chest, 121, 3, 906(15)
March,
2002
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0012-3692
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 11642 LINE COUNT: 01053

3/3,AB/4 (Item 4 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01922506 SUPPLIER NUMBER: 63713371 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Periodontal disease. (ABC of Oral Health)
Coventry, John; Griffiths, Gareth; Scully, Crispian; Tonetti, Maurizio
British Medical Journal, 321, 7252, 36
July 1,
2000
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0959-8146
LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE:
Professional
WORD COUNT: 2257 LINE COUNT: 00209

Searcher : Shears 308-4994

09/632657

ABSTRACT: Periodontal disease is a disease of the gums. It is usually caused by an accumulation of plaque on the teeth. The plaque irritates the gums, causing gingivitis. About 90% of the population has gingivitis to a certain degree, which manifests as bleeding during tooth brushing. Unless plaque is removed by tooth brushing and flossing, the condition will progress to periodontal disease. A pocket forms around teeth, and the erosion of bone will cause the tooth to fall out eventually. Proper dental hygiene is essential for preventing periodontal disease.

3/3,AB/5 (Item 5 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01919150 SUPPLIER NUMBER: 63255073 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Genetic factors and osteoporotic fractures in elderly people.(Letter to the Editor)

MacGregor, Alex J; Snieder, Harold; Spector, Tim D; Nemetz, Andrea; Pens, Amado Salvador; Kannus, Pekka; Kaprio, Jaakko; Koskenvuo, Markku; Palvanen, Mike; Parkkari, Jari
British Medical Journal, 320, 7250, 1669
June 17,
2000

DOCUMENT TYPE: Letter to the Editor PUBLICATION FORMAT: Magazine/Journal;
Refereed ISSN: 0959-8146 LANGUAGE: English RECORD TYPE: Fulltext
TARGET AUDIENCE: Professional
WORD COUNT: 1860 LINE COUNT: 00172

3/3,AB/6 (Item 6 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01900246 SUPPLIER NUMBER: 61635220 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Endothelial Apoptosis(*)

Stefanec, Tihomir
Chest, 117, 3, 841
March,
2000

PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0012-3692
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 10929 LINE COUNT: 01023

3/3,AB/7 (Item 7 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01890422 SUPPLIER NUMBER: 59961956 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Women and Tobacco: Oral Health Issues.

Fried, Jacquelyn L.
Journal of Dental Hygiene, 74, 1, 49
Wntr,
2000

PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 1043-254X
LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE:
Professional

Searcher : Shears 308-4994

09/632657

WORD COUNT: 5578 LINE COUNT: 00474

AUTHOR ABSTRACT: As a female-dominated profession, dental hygiene has a heightened interest in women's health issues. An area of disease prevention and health promotion that merits gender specific interventions is tobacco use. Tobacco initiation, habituation, and cessation are different for men and women, and their effects on women's health also are more varied and unique. This paper addresses trends in tobacco use by women, gender specific developmental and sociocultural considerations in initiation and habituation; the pregnant tobacco user and the developing fetus; *menopause***, osteoporosis, heart disease, and tobacco use; the economic impact of pregnancy and tobacco use; and successful interventions with women who use tobacco. Since women present for more dental office visits than males, female patients are more accessible to the dental hygienist's tobacco intervention message, and gender specific strategies may be most successful. Dental hygienists' strong counseling and motivational abilities, along with their inherent interest in women's issues, can make prevention and cessation activities with female patients who use tobacco both challenging and rewarding.

Key Words: Tobacco, pregnancy, tooth development, health promotion.

3/3,AB/8 (Item 8 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01889341 SUPPLIER NUMBER: 59643741 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Gene Therapy in Orthopaedics.
Evans, Christopher H.; Robbins, Paul D.
Orthopaedic Nursing, 19, 1, 16
Jan,
2000
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0744-6020
LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE:
Professional
WORD COUNT: 3647 LINE COUNT: 00316

AUTHOR ABSTRACT: Genes are composed of deoxyribonucleic acid (DNA), the hereditary material of all nucleated cells. One way in which genes function is to direct the synthesis of specific proteins. When a gene is transferred to and expressed within a cell, the recipient cell produces the protein encoded by the transferred gene. This process forms the basis for gene therapy, which can be defined as the transfer of genes to patients for therapeutic purposes. Both genetic and acquired disorders may be treated, or even cured, by gene therapy. Potential orthopaedic applications include the treatment of arthritis, tumors, osteoporosis, and genetic diseases such as osteogenesis imperfecta, as well as the enhancement of tissue repair and regeneration. Impressive preclinical progress has been made in several of these areas. A phase I clinical trial of gene therapy for rheumatoid arthritis has just been completed. Orthopaedic gene therapy should become a clinical reality during the next decade.

3/3,AB/9 (Item 9 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01887253 SUPPLIER NUMBER: 59579111 (USE FORMAT 7 OR 9 FOR FULL TEXT)

Searcher : Shears 308-4994

09/632657

Influence of vitamin D deficiency and vitamin D receptor *polymorphisms***
on tuberculosis among Gujarati Asians in west London: a case-control
study. (Statistical Data Included)

Wilkinson, Robert J; Llewelyn, Martin; Toossi, Zahra; Patel, Punita;
Pasvol, Geoffrey; Lalvani, Ajit; Wright, Dennis; Latif, Mohammed; Davidson,
Robert N

The Lancet, 355, 9204, 618
Feb 19,
2000

DOCUMENT TYPE: Statistical Data Included PUBLICATION FORMAT:
Magazine/Journal; Refereed ISSN: 0099-5355 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 4089 LINE COUNT: 00391

ABSTRACT: Vitamin D deficiency may contribute to the high occurrence of
tuberculosis in a population of Gujarati Asians living in London.
Susceptibility to disease from Mycobacterium tuberculosis infection is
influenced by environmental and host genetic factors, and vitamin D
metabolism restricts its growth. Of 126 untreated patients with
tuberculosis and 116 unrelated people without symptoms but who had
contacted and been sensitized to tuberculosis, active vitamin D metabolism
was recorded in 103 patients and 42 contacts. The levels were low in all
patients and significantly lower or completely undetectable in the patients
who had tuberculosis.

3/3,AB/10 (Item 10 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01862526 SUPPLIER NUMBER: 55941777 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Lichen sclerosus. (Seminar) (Statistical Data Included)

Powell, J J; Wojnarowska, F
The Lancet, 353, 9166, 1777
May 22,
1999

DOCUMENT TYPE: Statistical Data Included PUBLICATION FORMAT:
Magazine/Journal ISSN: 0099-5355 LANGUAGE: English RECORD TYPE:
Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 6271 LINE COUNT: 00515

ABSTRACT: The authors discuss the epidemiology of lichen sclerosis,
internationally accepted term for an inflammatory skin disease which is
also known as leucoplakia or lichen albus. It is a long-lasting, localized
inflammation which usually affects the anogenital area, and risk factors
for contracting it are not known. Treatment is difficult.

3/3,AB/11 (Item 11 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01802348 SUPPLIER NUMBER: 21245955 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Plasma levels of the soluble fraction of tumor necrosis factor receptor 2
and insulin resistance.

Fernandez-Real, Jose-Manuel; Broch, Montserrat; Ricart, Wifredo;
Casamitjana, Roser; Gutierrez, Cristina; Vendrell, Joan; Richart, Cristobal
Diabetes, v47, n11, p1757(6)

Searcher : Shears 308-4994

09/632657

Nov,
1998

PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0012-1797
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 5221 LINE COUNT: 00473

3/3,AB/12 (Item 12 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01765815 SUPPLIER NUMBER: 19731336 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Osteoarthritis. (review article)
Creamer, Paul; Hochberg, Marc C.
The Lancet, v350, n9076, p503(7)
August 16,
1997

PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0099-5355
LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE:
Professional
WORD COUNT: 6018 LINE COUNT: 00521

ABSTRACT: Osteoarthritis is a common form of arthritis characterized by a softening and loss of joint cartilage and possibly bone. It causes joint pain, tenderness, limitation of movement and may also have an inflammatory component. The risk increases with age and it usually affects the hands, knees, feet and hips. Obesity, occupation and sports participation are also risk factors. Pain can be treated with acetaminophen or non-steroidal anti-inflammatory drugs. Topical creams and corticosteroid joint injections may also be helpful. Physical therapy and joint replacement are other options.

3/3,AB/13 (Item 13 from file: 149)
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01750179 SUPPLIER NUMBER: 20318160 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Age-related response to interferon alfa treatment in women vs men with chronic hepatitis C virus infection.
Hayashi, Jun; Kishihara, Yasuhiro; Ueno, Kumiko; Yamaji, Kouzaburo;
Kawakami, Yasunobu; Furusyo, Norihiro; Sawayama, Yasunori; Kashiwagi, Seizaburo
Archives of Internal Medicine, v158, n2, p177(5)
Jan 26,
1998

PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0003-9926
LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE:
Professional
WORD COUNT: 4008 LINE COUNT: 00381

AUTHOR ABSTRACT: Background: Interferon alfa is used widely for patients with chronic hepatitis C virus (HCV) infection. Little is known, however, of the relationship between patients' sex and the effectiveness of interferon alfa treatment in these patients. Methods: We treated 311 patients (199 men and 112 women) with human lymphoblastoid interferon (6 million units subcutaneously every day for 2 weeks and 3 times a week for 22 weeks) and observed them for an additional 6 months. Serum HCV RNA

Searcher : Shears 308-4994

09/632657

levels and genotype were tested by polymerase chain reaction before treatment. A liver biopsy was also done. For the purposes of this study, a complete response was defined as the elimination of HCV RNA for at least 6 months after the termination of treatment. Results: The rate of complete response was 27.1% for men and 24.1% for women. With multiple logistic regression analysis, the HCV RNA level (P (is less than) .001), genotype (P (is less than) .001), patients' sex (P (is less than) .05), and the interaction between sex and age were associated with a complete response to interferon alfa. The rate of complete response was 33.3% in men aged 39 years and younger, 25.0% in men aged 40 years and older, 75.0% in women aged 39 years and younger, and 15.6% in women aged 40 years and older. The odds ratio by group was 1.00, 0.72, 4.38, and 0.21, respectively. Conclusions: Our finding that women aged 39 years and younger are responsive to interferon alfa treatment suggests that hormonal activity, in particular the level of estrogen, may be associated with the sustained elimination of HCV. Arch Intern Med. 1998;158:177-181

3/3,AB/14 (Item 14 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01717128 SUPPLIER NUMBER: 19748119 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Long-term effects of bisphosphonates on the growing skeleton: studies of young patients with severe osteoporosis.
Brumsen, Caro; Hamdy, Neveen A. T.; Papapoulos, Socrates E.
Medicine, v76, n4, p266(18)
July,
1997
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0025-7974
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 9060 LINE COUNT: 00774

3/3,AB/15 (Item 15 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01669298 SUPPLIER NUMBER: 18710785 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Cellular changes involved in conversion of normal to malignant breast: importance of the stromal reaction.
Ronnov-Jessen, Lone; Petersen, Ole W.; Bissell, Mina J.
Physiological Reviews, v76, n1, p69(57)
Jan,
1996
PUBLICATION FORMAT: Magazine/Journal ISSN: 0031-9333 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 48681 LINE COUNT: 03996

ABSTRACT: Breast cancer is characterized by a disorganization of the breast cells and a proliferation of stromal tissue throughout the breast. In the normal breast, a duct is surrounded by luminal epithelial cells that form into myoepithelial cells, which are then surrounded by a basal membrane. Studies of malignant breasts have found evidence that the stem cell for cancer may come from the myoepithelial cells, so that the duct is eventually blocked. Three types of carcinomas have been identified.

09/632657

3/3,AB/16 (Item 16 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01660977 SUPPLIER NUMBER: 18999122 (USE FORMAT 7 OR 9 FOR FULL TEXT)
*Polymorphism*** of the beta(sub 3)-adrenergic receptor gene affects basal
metabolic rate in obese Finns.
Sipilainen, Raisa; Uusitupa, Matti; Heikkinen, Sami; Rissanen, Aila;
Laakso, Markku
Diabetes, v46, n1, p77(4)
Jan,
1997
PUBLICATION FORMAT: Magazine/Journal ISSN: 0012-1797 LANGUAGE: English
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 3204 LINE COUNT: 00266

3/3,AB/17 (Item 17 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01659586 SUPPLIER NUMBER: 18943719 (USE FORMAT 7 OR 9 FOR FULL TEXT)
High frequency of BRCA1 185delAG *mutation*** in ovarian cancer in Israel.
Modan, Baruch; Gak, Eva; Sade-Bruchim, Revital Bar; Hirsh-Yechezkel, Galit;
Theodor, Livia; Lubin, Flora; Ben-Baruch, Gilad; Beller, Uzi; Fishman,
Amiram; Dgani, Ram; Menczer, Joseph; Papa, Moshe; Friedman, Eitan
JAMA, The Journal of the American Medical Association, v276, n22, p1823(3)
Dec 11,
1996
PUBLICATION FORMAT: Magazine/Journal ISSN: 0098-7484 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 2537 LINE COUNT: 00221

ABSTRACT: The presence of the 185delAG *mutation*** in the BRCA1 gene may
increase a woman's risk of developing ovarian cancer. The BRCA1 gene has
been linked to breast and ovarian cancer. Researchers tested for the gene
*mutation*** in 79 women with ovarian cancer, 62 women hospitalized for
other reasons and 120 healthy volunteers. Almost 40% of the ovarian cancer
patients with a family history had the *mutation***. Thirteen percent of
the ovarian cancer patients with no family history also had the
*mutation***. Only one person among the other two groups had the
*mutation***.

AUTHOR ABSTRACT: Objective.--To determine the role of BRCA1 185deIAG
*mutation*** in ovarian carcinogenesis. Design.--Genetic testing of a
subset of cases from an ongoing study of ovarian cancer and of controls.
Setting.--A community-based case-control incidence study.
Subjects.--Seventy-nine patients with ovarian cancer, 62 hospitalized women
without cancer (controls), and 120 healthy women participating in a fragile
X screening program (also controls), examined for the presence of germline
BRCA 1 185deIAG *mutation***. Main Outcome Measures.--Polymerase chain
reaction-amplified BRCA1 exon 2 fragments generated from patients' and
controls' blood samples, analyzed by heteroduplex gel shift assay and
direct sequence analyses. Results.--The 185deIAG *mutation*** was detected
in 38.9% (7/18) of ovarian cancer patients with familial history, and 13.1%
(8/61) of family history-negative ovarian cancer cases. Only 1 carder was
detected among the 120 healthy controls, and none in the hospital controls.
A significant difference in *mutation*** carrier rates between family
history-negative cases and control groups of 120 and 62 subjects was

Searcher : Shears 308-4994

09/632657

identified (Fisher exact test, $P=.001$ and $P=-.003$, respectively). The median age ((+or -)SE) at disease diagnosis was lower among both familial and family historynegative *mutation*** carriers, as compared with *mutation***-negative, family historynegative cases--50 ((+or -)1.4) vs 60.5 ((+or -)3.5) years old, respectively (hazard ratio, 1.68; 95% confidence interval, 0.94-3.01). Conclusions.-- Our data are preliminary but suggest that BRCA 1 185deIAG germline *mutation*** is frequent in Israeli ovarian cancer patients, irrespective of family history, and may confer an early-onset phenotype of ovarian cancer. JAMA. 1996;276:1823-1825

3/3,AB/18 (Item 18 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01620959 SUPPLIER NUMBER: 18371784 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Transcriptional control of osteoblast growth and differentiation.
Stein, Gary S.; Lian, Jane B.; Stein, Janet L.; Van Wijnen, Andre J.;
Montecino, Martin
Physiological Reviews, v76, n2, p593(37)
April,
1996
PUBLICATION FORMAT: Magazine/Journal ISSN: 0031-9333 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 33889 LINE COUNT: 02799

ABSTRACT: Osteoblasts undergo sequential stages of proliferation and mineralization in the process of development into bone. The proliferation stage is regulated by genes involve in initiating activation of mitosis, including c-fos, c-myc, c-jun, histones and cyclins. The development of the extracellular bone matrix is governed by genes encoding fibronectin, TGF-beta and type I collagen. The last stage, hydroxyapatite and collagenase deposition, is regulated by osteopontin and osteocalcin.

3/3,AB/19 (Item 19 from file: 149)
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01610139 SUPPLIER NUMBER: 18003876 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Florence Nightingale's fever. (Crimean fever)
Young, D.A.B.
British Medical Journal, v311, n7021, p1697(4)
Dec 23,
1995
PUBLICATION FORMAT: Magazine/Journal ISSN: 0959-8146 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 3259 LINE COUNT: 00271

ABSTRACT: Founder of modern nursing Florence Nightingale may have suffered from a bacterial infection she contracted during the Crimean War, which would explain her 25 years of convalescence. When no organic disease could be found, she was diagnosed with neurasthenia, which is associated with psychosomatic illness. Her symptoms included insomnia, anorexia, anemia, nervousness, and depression. Her doctors had recommended bed rest, and the nurse followed their advice. Nightingale may have been infected by brucella melitensis, which causes the disease brucellosis. Neurasthenia has been

09/632657

incorrectly diagnosed in cases of brucellosis. Nightingale's reputation has been tarnished by biographers who wrote that she was a malingerer who used her sickness for publicity.

3/3,AB/20 (Item 20 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01610114 SUPPLIER NUMBER: 17931220 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Osteoarthritis: a continuing challenge.
Sack, Kenneth E.
The Western Journal of Medicine, v163, n6, p579(8)
Dec,
1995
PUBLICATION FORMAT: Magazine/Journal ISSN: 0093-0415 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 7372 LINE COUNT: 00661

AUTHOR ABSTRACT: Osteoarthritis is a disorder of cartilage that affects almost 85% of the population by age 75. A lack of rigorous clinical and radiographic criteria for defining the disorder makes precise determination of its prevalence impossible. The process of wear and tear explains many manifestations of osteoarthritis, but it does not account for some of the clinical findings or the biochemical changes in osteoarthritic cartilage. Thus, other factors such as heredity, hormones, and diet may play a role. Treatment consists of teaching patients about their disease, alleviating pain, and preserving joint function. Nonsteroidal anti-inflammatory drugs may be no more effective than simple analgesics in relieving the pain of this disorder. Moreover, some nonsteroidal anti-inflammatory drugs can adversely affect cartilage metabolism, and most are possibly dangerous in elderly patients. Drugs that inhibit the production or activity of chondrolytic enzymes can slow the degeneration of cartilage in some animals, but their effects on humans with osteoarthritis are unproved. The surgical repair of severely damaged joints can have gratifying results.

3/3,AB/21 (Item 21 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01607615 SUPPLIER NUMBER: 17798844 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Genetic variation, nutrition, and chronic diseases. (Genetic Variation and Nutrition, part 2)
Simopoulos, Artemis P.
Nutrition Today, v30, n5, p194(13)
Sept-Oct,
1995
PUBLICATION FORMAT: Magazine/Journal ISSN: 0029-666X LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Consumer
WORD COUNT: 8286 LINE COUNT: 00707

AUTHOR ABSTRACT: This review of current knowledge of the role of genetic variation and nutrition in the prevention and treatment of chronic diseases builds on Part 1, which appeared in the August issue of Nutrition Today. General dietary recommendations are appropriate in countries where the basic problem is one of undernutrition. However, in Western societies, where overnutrition and sedentary lifestyles predominate, universal dietary

09/632657

recommendations for the prevention of chronic diseases are inappropriate. Rather, specific dietary recommendations targeted to the individual at risk based on family history and genetic predisposition are in order for both prevention and treatment of chronic diseases.

3/3,AB/22 (Item 22 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01605209 SUPPLIER NUMBER: 17623519 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Breast cancer: cause and prevention.(Review Article)
Hulka, Barbara S.; Stark, Azadeh T.
The Lancet, v346, n8979, p883(5)
Sept 30,
1995
PUBLICATION FORMAT: Magazine/Journal ISSN: 0099-5355 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 5067 LINE COUNT: 00416

ABSTRACT: The prevention of breast cancer is challenging current research efforts. Breast cancer is the most common cancer among women of the industrialized world. Some of the known causes include a family history of breast cancer, genetic and hormonal factors, dietary and nutritional aspects, lifestyle and environmental risks. Primary prevention aims to reduce identified breast cancer risks, such as limiting oral contraceptives and hormone replacement therapy. Tamoxifen, an anti-estrogen drug, seems to prevent cancer spread in some women and is currently undergoing testing. Pregnancy early in life may protect against breast cancer but fails to be a practical solution. Some lifestyle options are more feasible for the individual and include weight control, exercise, alcohol abstinence, vitamin A supplementation, and dietary fat reduction. Long-term nursing may not be an option for women in developed countries.

3/3,AB/23 (Item 23 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01364546 SUPPLIER NUMBER: 12448822 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Viseral obesity in men: associations with glucose tolerance, plasma insulin, and lipoprotein levels.
Pouliot, Marie-Christine; Despres, Jean-Pierre; Nadeau, Andre; Moorjani, Sital; Prud'Homme, Denis; Lupien, Paul J.; Tremblay, Angelo; Bouchard, Claude
Diabetes, v41, n7, p826(9)
July,
1992
PUBLICATION FORMAT: Magazine/Journal ISSN: 0012-1797 LANGUAGE: English
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 5067 LINE COUNT: 00528

3/3,AB/24 (Item 24 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01293058 SUPPLIER NUMBER: 10346593 (USE FORMAT 7 OR 9 FOR FULL TEXT)

09/632657

Overview of osteoporosis.

Riggs, B. Lawrence

The Western Journal of Medicine, v154, n1, p63(15)

Jan,

1991

PUBLICATION FORMAT: Magazine/Journal ISSN: 0093-0415 LANGUAGE: English

RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional

WORD COUNT: 10468 LINE COUNT: 01091

ABSTRACT: Osteoporosis occurs when there is decrease in the bone mass to a level where the bone can no longer the body. About 1.5 million fractures caused by osteoporosis occur in the United States each year, usually involving the hip, spine, or forearm. One in three women over 65 will suffer fractures of the spine, and 15 percent of white women, who are at higher risk, will suffer a hip fracture. The costs of these injuries is several billion dollars per year, and hip fractures are fatal in 12 to 20 percent of the cases. Fifty percent of the survivors never walk unaided again, and one in four must remain in a nursing home. This article reviews the process of bone formation and subsequent age-related loss, and the causes of osteoporosis. Osteoporosis in children and young adults is mentioned. A distinction is made between postmenopausal (type I) osteoporosis and osteoporosis caused by other factors, such as endocrine disorders (e.g., hyperthyroidism), gastrointestinal diseases (e.g., malabsorption diseases or anorexia), bone marrow disorders, connective tissue diseases, and others. The symptoms are described and the diagnostic procedure is outlined, including X-ray images. Drug therapy with estrogen is described, as well as calcium, vitamin D and calcitonin supplementation, and the use of biphosphonates, anabolic steroids, and sodium fluoride. Diet and exercise are mentioned but not stressed. Prevention is the only effective approach, and calcium intake should be at least 1,000 mg per day, perhaps more. Cigarettes and alcohol, both bone toxins, should be eliminated. The authors state that estrogen replacement beginning at *menopause*** is the most effective preventive, although this is highly controversial because of the increase in breast cancer and other ill effects. (Consumer Summary produced by Reliance Medical Information, Inc.)

3/3,AB/25 (Item 1 from file: 144)

DIALOG(R)File 144:Pascal

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15354424 PASCAL No.: 02-0041823

*Polymorphisms*** for *interleukin***-1*** beta (*IL***-1*** beta)-511 promoter, *IL***-1*** beta exon 5, and *IL***-1*** receptor antagonist : Nonassociation with endometriosis

HSIEH Yao-Yuan; CHANG Chi-Chen; TSAI Fuu-Jen; WU Jer-Yuarn; SHI Yi-Ru; TSAI Horng-Der; TSAI Chang-Hai

Department of Obstetrics and Gynecology, China Medical College Hospital, Taichung, Taiwan; Department of Pediatrics and Medical Genetics, China Medical College Hospital, Taichung, Taiwan

Journal: Journal of assisted reproduction and genetics, 2001, 18 (9) 506-511

Language: English

Purpose: We aimed to investigate if *interleukin***-1*** beta (*IL***-1*** beta) and *IL***-1*** receptor antagonist (IL-1Ra) gene *polymorphism*** could be used as markers of susceptibility in endometriosis. Materials and Methods: Women were divided into two groups: 1) endometriosis (n = 120); 2) nonendometriosis groups (n = 103).

Searcher : Shears 308-4994

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*Polymorphisms*** for *IL***-1*** beta -511 promoter, *IL***-1*** beta exon 5, and IL-1Ra were detected by polymerase chain reaction. Genotypes and allelic frequencies for these *polymorphisms*** in both groups were compared. Results: Proportions of different IL- I and IL- 1Ra *polymorphisms*** in both groups were nonsignificantly different. Proportions of C homozygote/heterozygote/T homozygote for *IL***-1*** beta -511 promoter in both groups were 1) 21.6/59.1/19.1% and 2) 26.2/50.5/23.3%. Proportions of E1 homozygote/ heterozygote/E2 homozygote for *IL***-1*** beta exon 5 in both groups were 1) 91.6/5/3.3% and 2) 95.15/4.85/0%. Allele I/ II/IV/V for IL-1Ra in both groups were 1) 92.5/5.4/1.6/0.4% and 2) 95.1/3.9/1/0%. Conclusions: Association of endometriosis with *IL***-1*** beta 511 promoter, *IL***-1*** beta exon 5, and *IL***-1*** receptor antagonist gene *polymorphisms*** doesn't exist. These *polymorphisms*** are not useful markers for prediction of endometriosis susceptibility.

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3/3,AB/26 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal
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13768522 PASCAL No.: 98-0481155

*Allelic*** *variation*** at the *interleukin***-1*** receptor antagonist gene is associated with early postmenopausal bone loss at the spine

KEEN R W; WOODFORD-RICHENS K L; LANCHBURY J S; SPECTOR T D

Twin & Genetic Epidemiology Research Unit, St. Thomas' Hospital, London, United Kingdom; Molecular Immunogenetics Unit, Thomas Guy House, UMDS, Guy's Hospital, London, United Kingdom

Journal: Bone : (New York), 1998, 23 (4) 367-371

Language: English

Genetic factors play an important role in determining bone mineral density (BMD) in later life, with the genetic influence mediated through effects on both peak mass and on age- and *menopause***-related bone loss. At *menopause*** there is an increase in the production and activity of various cytokines and growth factors within the bone microenvironment. The activity of *interleukin***-1*** (IL-I), a powerful stimulant of osteoclastic bone resorption, is increased in estrogen-deficient states with increased production of *IL***-1*** and inhibition of the *IL***-1*** receptor antagonist (IL-1ra). Treatment with IL-1ra blocks the bone loss associated with ovariectomy in animals and the *IL***-1*** receptor antagonist gene (*IL***-1RN***) is therefore a potential candidate gene for the regulation of postmenopausal bone loss. We examined the relationship between annual rates of change in BMD over 5 years and an 86 bp variable number tandem-repeat *polymorphism*** of the *IL***-1RN*** gene in 108 early postmenopausal women. All women were within 5 years of a natural *menopause*** at the study's onset, healthy, and not on hormone replacement therapy or other medication known to affect bone metabolism. BMD was measured annually over the 5 year study period at the lumbar spine and femoral neck using dual-energy X-ray absorptiometry. Three alleles were identified (A1 = 4 repeats, A2 = 2 repeats, A3 = 5 repeats), with five genotypes observed: A1A1 (41.7%), A1A2 (45.4%), A2A2 (6.5%), A1A3 (2.8%), and A2A3 (3.7%). For analysis, alleles were collapsed into a biallelic system grouping the A1 and A3 alleles. There was no significant relationship between the *IL***-1RN*** genotypes and baseline bone mass at either the spine or hip. *IL***-1RN*** genotype was significantly

Searcher : Shears 308-4994

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associated with annual rates of change in spinal bone mass ($p < 0.05$), and this finding remained significant after adjustment for age, weight, and baseline BMD. Carriage of at least one copy of the A2 allele was associated with reduced bone loss at the spine (mean change in BMD \pm SD: $-0.81 \pm 1.46\%$ /year) when compared with noncarriage of the A2 allele (mean change $-1.38 \pm 1.48\%$ /year), $p = 0.05$. We therefore conclude that *allelic*** *variation*** at the *IL***-1RN*** locus is associated with differential rates of early postmenopausal bone loss at the spine. Further research will be required to clarify the mechanisms underlying these findings and to determine whether this association translates into a significant long-term effect on BMD and fracture in later life.

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3/3,AB/27 (Item 1 from file: 76)
DIALOG(R)File 76:Life Sciences Collection
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02658351 5184984

Linkage of human tumor necrosis factor-alpha to human osteoporosis by sib-pair analysis

Ota, N.; Hunt, S.C.; Nakajima, T.; Suzuki, T.; Hosoi, T.; Orimo, H.; Shirai, Y.; Emi, M.

Department of Molecular Biology, Institute of Gerontology, Nippon Medical School, 1-396 Kosugi-cho, Nakahara-ku, Kawasaki 211-8533, Japan

Genes and Immunity vol. 1, no. 4, pp. 260-264 (2000)

ISSN: 1466-4879

DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH

SUBFILE: Genetics Abstracts; Immunology Abstracts

Osteoporosis as well as osteopenia are common human conditions considered to result from the interplay of multiple genetic and environmental factors. Twin and family studies have yielded strong correlation between measures of bone mass and a number of genetic factors. Certain genes (eg, cytokines such as *interleukin***-1***, interleukin-6, or tumor necrosis factor-alpha) are capable of regulating metabolism, formation, and resorption of bone all processes that determine bone mass. We tested 192 sib-pairs of adult Japanese women from 136 families for genetic linkage between osteoporosis and osteopenia phenotypes and *allelic*** *variants*** at the tumor necrosis factor-alpha (TNFA) locus, using a dinucleotide-repeat *polymorphism*** located near the gene. The TNFA locus showed evidence for linkage to osteoporosis, with mean allele sharing of 0.478 ($P = 0.30$) in discordant pairs and 0.637 ($P = 0.001$) in concordant affected pairs. Linkage with osteopenia was also significant in concordant affected pairs ($P = 0.017$). Analyses limited to the post-*menopausal*** women in our cohort showed similar or even stronger linkage for both phenotypes. The results provide evidence that genetic variations within the TNFA locus or adjacent genes affect regulation of mineral metabolism in bone and some of them confer risk for osteoporosis in adult women.

3/3,AB/28 (Item 2 from file: 76)
DIALOG(R)File 76:Life Sciences Collection
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Searcher : Shears 308-4994

09/632657

TGF- beta 1 stimulates expression of the aromatase (CYP19) gene in human osteoblast-like cells and THP-1 cells
Shozu, Makio; Zhao, Ying; Simpson, E.R.
Prince Henry's Institute for Medical Research, Monash Medical Centre, PO Box 5121, 246 Clayton Rd., Clayton, Vic 3168, Australia
Molecular and Cellular Endocrinology vol. 160, no. 1-2, pp. 123-133 (2000)
ISSN: 0303-7207
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Genetics Abstracts; Calcium & Calcified Tissue Abstracts

Recent evidence has shown that bone is not only a target of estrogen action but also a source of local estrogen production. Bone cells such as osteoblasts express aromatase (P450arom) and the expression of P450arom in osteoblasts is positively regulated in a tissue specific fashion, as in the case of other tissues which express P450arom. To clarify the physiological factors regulating expression of P450arom in bone, we tested TGF- beta 1 using osteoblast-like cells obtained from human fetuses as well as THP-1 cells. TGF- beta 1 increased *IL***-1*** beta +DEX- induced aromatase activity in osteoblast-like cells, while it inhibited activity in skin fibroblasts. Similar enhancement of aromatase activity by TGF- beta 1 was found in DEX-stimulated THP-1 cells and this cell line was used for further experiments. In THP-1 cells, TGF- beta 1 enhanced DEX-induced aromatase activity almost linearly by 12 h and thereafter. Increased levels of P450arom transcripts were also demonstrated by RT-PCR at 3 h of TGF- beta 1 treatment and thereafter. Cyclohexamide abolished enhancement of activity but did not inhibit the accumulation of P450arom transcripts induced by TGF- beta 1. Increase in P450arom expression by TGF- beta 1 was attributable to expression driven by promoter I.4. TGF- beta 1 did not change the half life of P450arom transcripts. To identify the cis-acting elements responsible for TGF- beta 1 action on aromatase expression, transient transfection assays were performed using a series of deletion constructs for promoter I.4 (P450-I.4/Luc). Two constructs (-410/+14 and -340/+14) that contain a functional glucocorticoid response element (GRE) and downstream sequence showed significant increase of luciferase activity in response to TGF- beta 1. Deletion and *mutation*** of the GRE in P450-I.4/Luc (-340/+14) abolished the TGF- beta 1. The luciferase activity of a (GRE) sub(1)-SV40/Luc construct was also stimulated by TGF- beta 1. These results indicate that TGF- beta 1 increases the expression of P450arom at the level of transcription through promoter I.4, at least in part via an enhancement of transactivation activity of the GR in THP-1 cells. TGF- beta 1 is suggested to be one of the physiological up-regulatory factors of bone aromatase.

3/3,AB/29 (Item 1 from file: 442)
DIALOG(R)File 442:AMA Journals
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00110821
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Phacoemulsification in Difficult and Challenging Cases - Foreign Body Entrapment in Radial Keratotomy Incisions (ARTICLE)

Archives of Ophthalmology
June, 1999; Case Reports and Small Case: tzh836
LINE COUNT: 00474

Searcher : Shears 308-4994

09/632657

3/3,AB/30 (Item 2 from file: 442)
DIALOG(R)File 442:AMA Journals
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00105596
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Autoimmune Endocrine Disease (ARTICLE)

BAKER, JAMES R.
JAMA, The Journal of the American Medical Association
December 10, 1997; 22: tzj1931
LINE COUNT: 00706

Autoimmune endocrine diseases are serious disorders that utilize immense health care resources and cause tremendous disability. They include type 1 diabetes mellitus, thyroiditis, Graves disease, Addison disease, and polyglandular syndromes. Analysis of the basis of autoimmune diseases has been aided by the application of new knowledge in immunologic physiology. Recent investigations using these techniques have revealed complicated disorders that have varied pathogenesis and complex genetic predispositions. While the mainstay of treatment for these diverse diseases remains the replacement of hormones produced by the damaged endocrine organ, investigations into the pathogenesis of these disorders provide hope for the development of specific therapeutic measures to block their pathologic basis. JAMA. 1997;278:1931-1937

3/3,AB/31 (Item 3 from file: 442)
DIALOG(R)File 442:AMA Journals
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00085620
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The Study of Gene-Environment Interactions That Influence Thrombosis and Fibrinolysis Genetic Variation at the Loci for Factor VII and Plasminogen Activator Inhibitor-1 (ARTICLE)

HUMPHRIES, STEVE E.; LANE, ANNE; DAWSON, SALLY; GREEN, FIONA R.
Archives of Pathology and Laboratory Medicine
December, 1992 Thrombosis--Humphries et al; p1322
LINE COUNT: 00679

We describe studies on variation in the genes coding for factor VII (FVII) and plasminogen activator inhibitor-1 (PAI-1) that influence levels of these proteins in the blood. For FVII, we have identified a genetic *polymorphism*** that results in the substitution of arginine at residue 353 to glutamine. The frequency of the glutamine allele is approximately 0.1 in samples of individuals from the United Kingdom (n=777) and the United States (n=140) and in Afro-Caribbeans (n=49), and is significantly higher in a sample of individuals from the Indian subcontinent (n=53). In all samples, carriers of the glutamine allele had levels of FVII coagulant activity 20% to 25% lower than those with only the arginine allele. These differences were highly statistically significant in the United Kingdom sample. This effect was consistent in healthy men and women and in those

with coronary artery disease. In individuals homozygous for the glutamine allele, both FVII coagulant activity and antigen are low, and the mechanism of the association appears likely to be due to an effect on secretion from the liver or stability in the plasma. In individuals in the general population FVII coagulant activity is positively correlated with levels of plasma triglycerides, due to the effect of such lipoproteins on activation of FVII. This relationship appears weaker in individuals carrying the glutamine allele, and since elevated FVII coagulant antibody is associated with risk of thrombosis, this is an example of how environmental factors may interact with an individual's genotype to determine his or her thrombotic risk. Roughly 20% of the general population are carriers of the glutamine allele and are likely to be genetically protected from such risk. For PAI-1, we have recently shown that variation at the PAI gene locus, detected as DNA "polymorphisms"***, is associated with between-individual differences in levels of PAI-1. We have now detected a common sequence change in the promoter region of the gene that explains part of this effect. The sequence change is at position 675, where a fifth guanine (5G allele) has been inserted into a run of four guanines (4G allele) when compared with published sequences. In a sample of both 83 healthy individuals and 105 young patients with coronary artery disease from Sweden, the frequency of the 4G allele is roughly 0.5, and those individuals homozygous for the 4G allele have higher levels of PAI-1 than those with other genotypes (29% higher). Preliminary data show that the 5G allele binds a hepatic nuclear protein that the 4G allele does not, suggesting that the mechanism of the effect may be due to a direct effect of the sequence change on transcription of the PAI-1 gene. Expression of the PAI-1 gene is known to be modulated by cytokines produced in the acute-phase response, and statistical analysis shows evidence for a strongly positive relationship between PAI-1 levels and markers of the acute phase in individuals with the genotype 4G/4G (correlation with fibrinogen, 0.33 in patients, 0.42 in healthy group) and a weaker or negative relationship in those with other genotypes (for the 5G/5G group, -0.35, and -0.18, respectively). These differences were statistically significant in the healthy group, and represent a second situation where interaction between environmental factors and genetic variation may be important in determining an individual's levels of PAI-1 over time and thus risk of a thrombotic event due to reduced fibrinolytic potential. (Arch Pathol Lab Med. 1992;116:)

3/3, AB/32 (Item 4 from file: 442)
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00085617
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Thrombosis and Cardiovascular Risk in the Elderly (ARTICLE)

TRACY, RUSSELL P.
 Archives of Pathology and Laboratory Medicine
 December, 1992; Original Article: p1307
 LINE COUNT: 00557

Current concepts of cardiovascular disease pathophysiology include a prominent role for thrombosis as a key factor. Thrombosis is not only the usual precipitant to a clinical event, but it may also be involved in atherosclerotic plaque development throughout most of the adult years. However, our understanding of thrombotic risk factors, especially in the

09/632657

elderly, is poor and research has just begun in this area. Fibrinogen has been clearly established as an independent risk factor in the middle aged, but there are conflicting data concerning older persons. Factor VII and plasminogen activator inhibitor-1 look promising as risk factors in the middle aged, but there are no data currently available concerning the status of these factors in the elderly. Many associations exist between the thrombotic risk factors and other cardiovascular risk factors such as plasma lipids and glucose intolerance, making the establishment of independence difficult, and little is known about how these different factors may interact in older individuals. Ongoing studies should provide many answers in the near future. (Arch Pathol Lab Med. 1992;116:)

3/3,AB/33 (Item 5 from file: 442)
DIALOG(R)File 442:AMA Journals
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00025544
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Glucan-Induced Keratoderma in Acquired Immunodeficiency Syndrome (STUDIES)

DUVIC, MADELEINE; REISMAN, MARK; FINLEY, VICTORIA; RAPINI, RONALD;
DILUZIO, NICHOLAS R.; MANSELL, PETER W. A.
Archives of Dermatology
June, 1987; 123: 751-756
LINE COUNT: 00204 WORD COUNT: 02828

ABSTRACT: Six of 20 patients with acquired immunodeficiency syndrome (AIDS) or AIDS-related complex receiving intravenous infusions of soluble glucan (beta-1-3 polyglucose) developed a keratoderma of the palms and soles. The eruption began during the first two weeks of therapy and resolved two to four weeks after its discontinuation. The eruption was different in appearance from our previously reported keratoderma blennorrhagica in AIDS-associated psoriasis. None of the other 735 patients with AIDS or AIDS-related complex not treated with soluble glucan developed a similar keratoderma. The correlation between receiving glucan and the hyperkeratosis is highly significant. Since glucan is a naturally occurring component of the cell walls of yeast, fungus, and some bacterial organisms, recognition of its ability to induce such a striking reaction pattern may be of general significance and interest, although the reaction itself may be limited to patients with AIDS.

3/3,AB/34 (Item 1 from file: 444)
DIALOG(R)File 444:New England Journal of Med.
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00122140
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Mechanisms of Disease: Production and Actions of Estrogens (Review Article)

Gruber, Christian J.; Tschugguel, Walter; Schneeberger, Christian;
Huber, Johannes C.
The New England Journal of Medicine
Jan 31, 2002; 346 (5),pp 340-352

Searcher : Shears 308-4994

09/632657

LINE COUNT: 00466

WORD COUNT: 06443

3/3,AB/35 (Item 2 from file: 444)
DIALOG(R)File 444:New England Journal of Med.
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00120379

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Mechanisms of Disease: Plasminogen-Activator Inhibitor Type 1 and Coronary Artery Disease (Review Articles)

Kohler, Hans P.; Grant, Peter J.
The New England Journal of Medicine
Jun 15, 2000; 342 (24),pp 1792-1801
LINE COUNT: 00467 WORD COUNT: 06450

3/3,AB/36 (Item 3 from file: 444)
DIALOG(R)File 444:New England Journal of Med.
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00120065

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Cytokeratin-Positive Cells in the Bone Marrow and Survival of Patients with Stage I, II, or III Breast Cancer (Original Articles)

Braun, Stephan; Pantel, Klaus; Muller, Peter; Janni, Wolfgang; Hepp, Florian; Kentenich, Christina R.M.; Gastroph, Stephan; Wischnik, Artur; Dimpfl, Thomas; Kindermann, Gunter; Riethmuller, Gert; Schlimok, Gunter.
The New England Journal of Medicine
Feb 24, 2000; 342 (8),pp 525-533
LINE COUNT: 00378 WORD COUNT: 05223

Abstract

Background: Cytokeratins are specific markers of epithelial cancer cells in bone marrow. We assessed the influence of cytokeratin-positive micrometastases in the bone marrow on the prognosis of women with breast cancer.

Methods: We obtained bone marrow aspirates from both upper *iliac*** crests of 552 patients with stage I, II, or III breast cancer who underwent complete resection of the tumor and 191 patients with nonmalignant disease. The specimens were stained with the monoclonal antibody A45-B/B3, which binds to an antigen on cytokeratins. The median follow-up was 38 months (range, 10 to 70). The primary end point was survival.

Results: Cytokeratin-positive cells were detected in the bone marrow specimens of 2 of the 191 control patients with nonmalignant conditions (1 percent) and 199 of the 552 patients with breast cancer (36 percent). The presence of occult metastatic cells in bone marrow was unrelated to the presence or absence of lymph-node metastasis ($P=0.13$). After four years of follow-up, the presence of micrometastases in bone marrow was associated with the occurrence of clinically overt distant metastasis and death from cancer-related causes ($P<0.001$), but not with locoregional relapse ($P=0.77$). Of 199 patients with occult metastatic cells, 49 died of cancer, whereas of 353 patients without such cells, 22 died of cancer-related

09/632657

causes ($P < 0.001$). Among the 301 women without lymph-node metastases, 14 of the 100 with bone marrow micrometastases died of cancer-related causes, as did 2 of the 201 without bone marrow micrometastases ($P < 0.001$). The presence of occult metastatic cells in bone marrow, as compared with their absence, was an independent prognostic indicator of the risk of death from cancer (relative risk, 4.17; 95 percent confidence interval, 2.51 to 6.94; $P < 0.001$), after adjustment for the use of systemic adjuvant chemotherapy.

Conclusions: The presence of occult cytokeratin-positive metastatic cells in bone marrow increases the risk of relapse in patients with stage I, II, or III breast cancer. (N Engl J Med 2000;342:525-33.)

3/3,AB/37 (Item 4 from file: 444)
DIALOG(R)File 444:New England Journal of Med.
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00119835
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Metastasizing Aggressive Angiomyxoma (Correspondence)

Siassi, Ramin Michael; Papadopoulos, Thomas; Matzel, Klaus E.
The New England Journal of Medicine
Dec 2, 1999; 341 (23),p 1772
LINE COUNT: 00049 WORD COUNT: 00681

3/3,AB/38 (Item 5 from file: 444)
DIALOG(R)File 444:New England Journal of Med.
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00117127
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Brief Report: Effect of Testosterone and Estradiol in a Man with Aromatase Deficiency (Original Articles)

Carani, Cesare; Qin, Kenan; Simoni, Manuela; Faustini-Fustini, Marco;
Serpente, Stefania; Boyd, Jeff; Korach, Kenneth S.; Simpson, Evan R.
The New England Journal of Medicine
Jul 10, 1997; 337 (2),pp 91-95
LINE COUNT: 00324 WORD COUNT: 04477

3/3,AB/39 (Item 6 from file: 444)
DIALOG(R)File 444:New England Journal of Med.
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00116949
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Seminars in Medicine of the Beth Israel Deaconess Medical Center:
Neuroendocrine Responses to Starvation and Weight Loss (Review Article)

Schwartz, Michael W.; Seeley, Randy J.
The New England Journal of Medicine
Jun 19, 1997; 336 (25),pp 1802-1811
LINE COUNT: 00565 WORD COUNT: 07803

09/632657

3/3,AB/40 (Item 7 from file: 444)
DIALOG(R)File 444:New England Journal of Med.
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00116161
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Bone Mineral Density in Women with Depression (Original Articles)

Michelson, David; Stratakis, Constantine; Hill, Lauren; Reynolds,
James; Galliven, Elise; Chrousos, George; Gold, Philip.
The New England Journal of Medicine
Oct 17, 1996; 335 (16),pp 1176-1181
LINE COUNT: 00241 WORD COUNT: 03333

Abstract

Background: Depression is associated with alterations in behavior and neuroendocrine systems that are risk factors for decreased bone mineral density. This study was undertaken to determine whether women with past or current major depression have demonstrable decreases in bone density.

Methods: We measured bone mineral density at the hip, spine, and radius in 24 women with past or current major depression and 24 normal women matched for age, body-mass index, *menopausal*** status, and race, using dual-energy x-ray absorptiometry. We also evaluated cortisol and growth hormone secretion, bone metabolism, and vitamin D-receptor alleles.

Results: As compared with the normal women, the mean (+/-SD) bone density in the women with past or current depression was 6.5 percent lower at the spine (1.00 ± 0.15 vs. 1.07 ± 0.09 g per square centimeter, $P = 0.02$), 13.6 percent lower at the femoral neck (0.76 ± 0.11 vs. 0.88 ± 0.11 g per square centimeter, $P < 0.001$), 13.6 percent lower at Ward's triangle (0.70 ± 0.14 vs. 0.81 ± 0.13 g per square centimeter, $P < 0.001$), and 10.8 percent lower at the trochanter (0.66 ± 0.11 vs. 0.74 ± 0.08 g per square centimeter, $P < 0.001$). In addition, women with past or current depression had higher urinary cortisol excretion (71 ± 29 vs. 51 ± 19 microg per day 196 ± 80 vs. 141 ± 52 nmol per day], $P = 0.006$), lower serum osteocalcin concentrations ($P = 0.04$), and lower urinary excretion of deoxypyridinoline ($P = 0.02$).

Conclusions: Past or current depression in women is associated with decreased bone mineral density. (N Engl J Med 1996;335:1176-81.)

3/3,AB/41 (Item 8 from file: 444)
DIALOG(R)File 444:New England Journal of Med.
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00114230
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Medical Progress: Recent Advances in Radiation Oncology (Review Article)

Lichter, Allen S.; Lawrence, Theodore S.
The New England Journal of Medicine
Feb 9, 1995; 332 (6),pp 371-379
LINE COUNT: 00498 WORD COUNT: 06882

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3/3,AB/42 (Item 9 from file: 444)
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00108615

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Hyperhomocysteinemia: An Independent Risk Factor For Vascular Disease
(Original Articles)

Clarke, Robert; Daly, Leslie; Robinson, Killian; Naughten, Eileen;
Cahalane, Seamus; Fowler, Brian; Graham, Ian.
The New England Journal of Medicine
Apr 25, 1991; 324 (17),pp 1149-1155
LINE COUNT: 00375 WORD COUNT: 05183

Abstract

Background. Hyperhomocysteinemia arising from impaired methionine metabolism, probably usually due to a deficiency of cystathionine beta-synthase, is associated with premature cerebral, peripheral, and possibly coronary vascular disease. Both the strength of this association and its independence of other risk factors for cardiovascular disease are uncertain. We studied the extent to which the association could be explained by heterozygous cystathionine beta-synthase deficiency.

Methods. We first established a diagnostic criterion for hyperhomocysteinemia by comparing peak serum levels of homocysteine after a standard methionine-loading test in 25 obligate heterozygotes with respect to cystathionine beta-synthase deficiency (whose children were known to be homozygous for homocystinuria due to this enzyme defect) with the levels in 27 unrelated age- and sex-matched normal subjects. A level of 24.0 micromol per liter or more was 92 percent sensitive and 100 percent specific in distinguishing the two groups. The peak serum homocysteine levels in these normal subjects were then compared with those in 123 patients whose vascular disease had been diagnosed before they were 55 years of age.

Results. Hyperhomocysteinemia was detected in 16 of 38 patients with cerebrovascular disease (42 percent), 7 of 25 with peripheral vascular disease (28 percent), and 18 of 60 with coronary vascular disease (30 percent), but in none of the 27 normal subjects. After adjustment for the effects of conventional risk factors, the lower 95 percent confidence limit for the odds ratio for vascular disease among the patients with hyperhomocysteinemia, as compared with the normal subjects, was 3.2. The geometric-mean peak serum homocysteine level was 1.33 times higher in the patients with vascular disease than in the normal subjects ($P = 0.002$). The presence of cystathionine beta-synthase deficiency was confirmed in 18 of 23 patients with vascular disease who had hyperhomocysteinemia.

Conclusions. Hyperhomocysteinemia is an independent risk factor for vascular disease, including coronary disease, and in most instances is probably due to cystathionine beta-synthase deficiency. (N Engl J Med 1991; 324:1149-55.)

3/3,AB/43 (Item 10 from file: 444)
DIALOG(R)File 444:New England Journal of Med.
(c) 2002 Mass. Med. Soc. All rts. reserv.

00104423

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09/632657

Case 13-1988: Pelvic Mass in a 42-Year-Old Woman with a History of Salmonella Sepsis (Case Records of the Massachusetts General Hospital)

Stubblefield, Phillip G.; Bell, Debra A.
The New England Journal of Medicine
March 31, 1988; 318 (13), pp 835-842
LINE COUNT: 00638 WORD COUNT: 08804

3/3,AB/44 (Item 1 from file: 16)
DIALOG(R)File 16:Gale Group PROMT(R)
(c) 2002 The Gale Group. All rts. reserv.

08927282 Supplier Number: 77416504
PART II Prescription for success.(pharmaceuticals in development)(Illustration)
News, Med Ad
Med Ad News, v20, n7, pNA
July, 2001
Language: English Record Type: Fulltext
Article Type: Illustration
Document Type: Magazine/Journal; Trade
Word Count: 34591

3/3,AB/45 (Item 2 from file: 16)
DIALOG(R)File 16:Gale Group PROMT(R)
(c) 2002 The Gale Group. All rts. reserv.

08927281 Supplier Number: 77416502
PART I Prescription for success.(developing new pharmaceuticals)(Illustration)
News, Med Ad
Med Ad News, v20, n7, p3
July, 2001
Language: English Record Type: Fulltext
Article Type: Illustration
Document Type: Magazine/Journal; Trade
Word Count: 27870

3/3,AB/46 (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text
(c) 2002 The HW Wilson Co. All rts. reserv.

04755389 H.W. WILSON RECORD NUMBER: BGSA02005389
Aromatase--a brief overview.
Simpson, Evan R
Clyne, Colin; Rubin, Gary
Annual Review of Physiology v. 64 (2002) p. 93-127
SPECIAL FEATURES: bibl il ISSN: 0066-4278
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: 16532

ABSTRACT: There is growing awareness that androgens and estrogens have general metabolic roles that are not directly involved in reproductive processes. These include actions on vascular function, lipid and

Searcher : Shears 308-4994

09/632657

carbohydrate metabolism, as well as bone mineralization and epiphyseal closure in both sexes. In postmenopausal women, as in men, estrogen is no longer solely an endocrine factor but instead is produced in a number of extragonadal sites and acts locally at these sites in a paracrine and intracrine fashion. These sites include breast, bone, vasculature, and brain. Within these sites, aromatase action can generate high levels of estradiol locally without significantly affecting circulating levels. Circulating C19 steroid precursors are essential substrates for extragonadal estrogen synthesis. The levels of these androgenic precursors decline markedly with advancing age in women, possible from the mid-to-late reproductive years. This may be a fundamental reason why women are at increased risk for bone mineral loss and fracture, and possibly decline of cognitive function, compared with men. Aromatase expression in these various sites is under the control of tissue-specific promoters regulated by different cohorts of transcription factors. Thus in principle, it should be possible to develop selective aromatase modulators (SAMs) that block aromatase expression, for example, in breast, but allow unimpaired estrogen synthesis in other tissues such as bone. Reprinted by permission of the publisher.

3/3,AB/47 (Item 2 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text
(c) 2002 The HW Wilson Co. All rts. reserv.

04265301 H.W. WILSON RECORD NUMBER: BGSA00015301
Leptin.
Ahima, Rexford S
Flier, Jeffrey S
Annual Review of Physiology v. 62 (2000) p. 413-37
SPECIAL FEATURES: bibl il ISSN: 0066-4278
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: 12386

ABSTRACT: The discovery of the adipose-derived hormone leptin has generated enormous interest in the interaction between peripheral signals and brain targets involved in the regulation of feeding and energy balance. Plasma leptin levels correlate with fat stores and respond to changes in energy balance. It was initially proposed that leptin serves a primary role as an anti-obesity hormone, but this role is commonly thwarted by leptin resistance. Leptin also serves as a mediator of the adaptation to fasting, and this role may be the primary function for which the molecule evolved. There is increasing evidence that leptin has systemic effects apart from those related to energy homeostasis, including regulation of neuroendocrine and immune function and a role in development. With permission, from the Annual Review of Physiology Volume 62, 2000, by Annual Reviews Inc. (<http://www.annurev.org>).

3/3,AB/48 (Item 1 from file: 156)
DIALOG(R)File 156:ToxFile
(c) 2002. All rts. reserv.

01165002 97133753 PMID: 8979148
Estriol: a potent regulator of TNF and IL-6 expression in a murine model of endotoxemia.
Zuckerman SH; Ahmari SE; Bryan-Poole N; Evans GF; Short L; Glasebrook AL

Searcher : Shears 308-4994

09/632657

Division of Cardiovascular Research, Lilly Research Labs, Indianapolis, Indiana 46285, USA.

Inflammation (UNITED STATES) Dec 1996, 20 (6) p581-97, ISSN 0360-3997 Journal Code: GM0

Document type: Journal Article

Languages: ENGLISH

The increased incidence of autoimmune disease in *premenopausal*** women suggests the involvement of sex steroids in the pathogenesis of these disease processes. The effects of estrogen on autoimmunity and inflammation may involve changes in the secretion of inflammatory mediators by mononuclear phagocytes. Estradiol, for example, has been reported to regulate TNF, IL-6, *IL***-1*** and JE expression. In the present study the effects of the estrogen agonist, estriol, on cytokine expression have been investigated in mice administered a sublethal lipopolysaccharide, LPS, challenge. Pretreatment of mice with pharmacologic doses of estriol, 0.4-2 mg/kg, resulted in a significant increase in serum TNF levels in both control and autoimmune MRL/lpr mice, following LPS challenge. This increase in TNF over the placebo group was blocked by the estrogen antagonist tamoxifen. Estriol treated mice also exhibited a rapid elevation in serum IL-6 levels following LPS challenge with the peak increase occurring 1 hr post LPS. This contrasted with the placebo group in which maximal serum IL-6 levels were detected at 3 hrs post challenge. This shift in the kinetics of IL-6 increase by estriol was inhibited by tamoxifen. The estriol mediated effects of TNF and IL-6 serum levels were consistent with the changes in TNF and IL-6 mRNA observed ex vivo in elicited peritoneal macrophages. Macrophage cultures from estriol treated animals however, did not demonstrate significant differences from the placebo group for TNF or NO secretion following in vitro LPS challenge. These results suggest that the estrogen agonist estriol can have significant quantitative, TNF, and kinetic, IL-6, effects on inflammatory monokines produced in response to an endotoxin challenge.

3/3,AB/49 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online
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01833738 AADAAIC805829

Osteoprotegerin in bone metabolism

Author: Brandstrom, Helena Ingrid

Degree: Ph.D.

Year: 2001

Corporate Source/Institution: Uppsala Universitet (Sweden) (0903)

Source: VOLUME 62/03-C OF DISSERTATION ABSTRACTS INTERNATIONAL.

PAGE 404. 56 PAGES

ISBN: 91-554-5016-4

Publisher: Uppsala University Library, Sweden

Bone turnover, remodeling, is a constant process replacing old bone with new. This complex cellular event involves resorption by osteoclasts and formation of new bone by osteoblasts. The balance between osteoblastic and osteoclastic activity is under regulation by several endocrine and paracrine factors. Osteoprotegerin (OPG), a recently discovered protein is an effective inhibitor of osteoclast formation and osteoclast activity. In this thesis, the regulation of OPG mRNA expression and protein secretion from human bone cells has been investigated. Also correlation between a single nucleotide *polymorphism*** in the OPG gene and bone mass has been studied. OPG mRNA levels were affected by several endocrine and paracrine

Searcher : Shears 308-4994

09/632657

factors known to regulate bone resorption, such as prostaglandin E₂, TNFs, *interleukin*-1 and glucocorticoid. An ELISA was developed and it was established that human osteoblasts secrete OPG protein and that the secretion is regulated by the above factors. A single nucleotide *polymorphism* was discovered in the human OPG gene. There was no correlation between the *polymorphism* and measures of bone mineral density in a cohort of 1044 post-*menopausal* females. Surprisingly, a correlation between the *polymorphism* and measures of vascular function and morphology was discovered. The data in the thesis show that OPG is produced in human bone marrow and is regulated by factors affecting the bone remodeling process, suggesting a central role for OPG in human bone turnover. The finding that the *polymorphism* in the OPG gene correlates with vascular function opens up a new area of research aiming at understanding whether OPG might be involved also in cardiovascular diseases.

3/3,AB/50 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences
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03405329 INSIDE CONFERENCE ITEM ID: CN035948375
IL-1 Receptor Antagonist Gene *Polymorphism* Associated with Age of *Menopause*

van Dijk, S.; Stone, K. L.; Hannon, R. A.; Lui, L. L.; Sorrell, J. A.; Eastell, R.; Cummings, S. R.; Duff, G. W.

CONFERENCE: American Society for Bone and Mineral Research-Annual meeting; 22nd

JOURNAL OF BONE AND MINERAL RESEARCH, 2000; VOL 15; SUPPL 1 P: M341
Blackwell Science, 2000

ISSN: 0884-0431

LANGUAGE: English DOCUMENT TYPE: Conference Preprinted abstracts and programme

CONFERENCE SPONSOR: American Society for Bone and Mineral Research

CONFERENCE LOCATION: Toronto, Canada

CONFERENCE DATE: Sep 2000

Set	Items	Description
S4	378	AU=(DUFF, G? OR DUFF G?)
S5	76	AU=(KORNMAN, K? OR KORNMAN K?)
S6	63	AU=(VAN DIJK, S? OR VAN DIJK S? OR VANDIJK, S? OR VANDIJK - S?)
S7	0	S4 AND S5 AND S6
S8	5	S4 AND (S5 OR S6)
S9	1	S5 AND S6
S10	1	(S4 OR S5 OR S6) AND S1
S11	5	(S8 OR S9 OR S10) NOT S2
S12	5	RD (unique items)

>>>No matching display code(s) found in file(s): 65, 129, 158, 624

12/3,AB/1 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
(c) 2002 INIST/CNRS. All rts. reserv.

14606426 PASCAL No.: 00-0275153

Effect of interleukin-1 gene polymorphisms on gingival inflammation assessed by bleeding on probing in a periodontal maintenance population

LANG N P; TONETTI M S; SUTER J; SORRELL J; *DUFF G W***; *KORNMAN K S***

Searcher : Shears 308-4994

09/632657

Department of Periodontology and Fixed Prosthodontics, University of Berne, Switzerland; Department of Periodontology, Eastman Dental Institute, University College London, United Kingdom; Division of Molecular and Genetic Medicine, University of Sheffield, United Kingdom; Interleukin Genetics, San Antonio, Texas, United States

Journal: Journal of periodontal research, 2000, 35 (2) 102-107

Language: English

Bleeding on probing (BOP) is the most significant clinical parameter for the assessment of periodontal inflammation. The aim of this prospective longitudinal trial was to study the association between allelic variants of the IL-1 gene complex and gingival inflammation. Three hundred and twenty-three randomly selected periodontal maintenance patients (64.4% females) received a periodontal examination that included probing depth measurements and BOP at each of 4 supportive periodontal therapy (SPT) appointments. A blood sample taken from each subject was analysed for the presence of specific allotypes of the IL-1 gene complex. Two polymorphisms located at + 4845 bp in the IL-1 alpha region and at + 3954 bp in the IL-1 beta region were evaluated by a polymerase chain reaction method; 35.3% of the examined subjects were positive for specific combinations of allotypes of the IL-1 gene complex previously associated with an increased risk for severe periodontitis. The population consisted of 90 current smokers and 94 former smokers. An analysis of the association between the IL-1 genotype and BOP in the whole population (including smokers) did not reach statistical significance because of the overriding effect of smoking. A subset analysis of the 139 never smokers indicated that genotype positive patients had a significantly elevated chance of presenting an increase in the BOP% over a 4-appointment recall period ($p=0.03$) after correcting for oral hygiene. In fact, patients who were genotype-negative had a 50% smaller chance of showing increases in BOP% during SPT. A further analysis explored the relationship between the genotype and the level of BOP% at the most recent recall visit. A generalized linear model showed a statistically significant effect of the genotype status after correcting for plaque accumulation and prevalence of residual pockets (≥ 5 mm). Genotype-negative subjects had significantly lower BOP% ($p=0.0097$). It is concluded that the increased BOP prevalence and incidence observed in IL-1 genotype-positive subjects indicates that some individuals have a genetically determined hyper-inflammatory response that is expressed in the clinical response of the periodontal tissues.

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12/3,AB/2 (Item 1 from file: 76)
DIALOG(R)File 76:Life Sciences Collection
(c) 2002 Cambridge Sci Abs. All rts. reserv.

02708052 5371725

A Sequence-Based Map of the Nine Genes of the Human Interleukin-1 Cluster
Nicklin, M.J.; Barton, J.L.; Nguyen, M.; Fitzgerald, M.G.; *Duff, G.W.**;
*Kornman, K.**

Division of Genomic Medicine, University of Sheffield, Royal Hallamshire
Hospital, Sheffield, S10 2JF, UK

Genomics vol. 79, no. 5, pp. 718-725 (2002)

ISSN: 0888-7543

DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH

SUBFILE: Genetics Abstracts

Six novel genes encoding proteins with the interleukin (IL)-1 fold have been identified recently. The classical family members are involved in

09/632657

inflammatory signaling. Previous work has placed the novel genes close to or within the same cluster as IL1A, IL1B, and IL1RN, which occupy an similar to 400-kb interval on chromosome 2. We have combined the incomplete public database sequence with our own sequence to generate a reference sequence and map that encompass all of the novel genes, allowing determination of the gene structures, precise localization of exons, and determination of distances between conventional SNP and microsatellite markers. Gene order from centromere to telomere is IL1A-IL1B-IL1F7-IL1F9-IL1F6-IL1F8-IL1F5-IL1F10-IL1RN, of which only IL1A, IL1B, and IL1F8 are transcribed towards the centromere. The gene order relates to the evolutionary relationship between the genes. Key features of exon boundaries are conserved. There is no evidence for other IL-1 family members within the cluster. [copy] 2002 Elsevier Science (USA).

12/3,AB/3 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences
(c) 2002 BLDSC all rts. reserv. All rts. reserv.

04052822 INSIDE CONFERENCE ITEM ID: CN042595834
Candidate Genes as Potential Links Between Periodontal and Cardiovascular Diseases

*Kornman, K. S."**; *Duff, G. W."**
CONFERENCE: Periodontal-systemic connection: a state-of-the-science symposium
ANNALS OF PERIODONTOLOGY, 2001; VOL 6; NO 1 P: 48-57
American Academy of periodontology, 2001
LANGUAGE: English DOCUMENT TYPE: Conference Papers. described as proceedings
CONFERENCE SPONSOR: American Association of Periodontology
National Institute of Dental and Craniofacial Research
CONFERENCE LOCATION: Bethesda, MD 2001; Apr (200104) (200104)

12/3,AB/4 (Item 2 from file: 65)
DIALOG(R)File 65:Inside Conferences
(c) 2002 BLDSC all rts. reserv. All rts. reserv.

03122730 INSIDE CONFERENCE ITEM ID: CN033103270
Interleukin-1 genotypes and the association between periodontitis and cardiovascular disease

*Kornman, K. S."**; Pankow, J.; Offenbacher, S.; Beck, J.; di Giovine, F.; *Duff, G. W."**
CONFERENCE: Periodontal research-International conference; 11th
JOURNAL OF PERIODONTAL RESEARCH, 1999; VOL 34; NO 7 P: 353-357
Munksgaard, 1999
ISSN: 0022-3484
LANGUAGE: English DOCUMENT TYPE: Conference Papers
CONFERENCE LOCATION: Gothenburg, Sweden
CONFERENCE DATE: Jun 1999 (199906) (199906)

12/3,AB/5 (Item 3 from file: 65)
DIALOG(R)File 65:Inside Conferences
(c) 2002 BLDSC all rts. reserv. All rts. reserv.

02636424 INSIDE CONFERENCE ITEM ID: CN027455640
IL-1 Receptor Antagonist as a Potential New Therapeutic Agent for

Searcher : Shears 308-4994

09/632657

Osteoporosis: A Computer Simulation Model of Bone Remodeling and Osteoporosis

Herren, L. T.; *Van Dijk, S."**; Wang, H. Y.; *Kornman, K. S."**

CONFERENCE: American Society for Bone and Mineral Research and International Bone and Mineral Society: ASBMR-IBMS second joint meeting-Joint meeting; 2nd

BONE -NEW YORK-, 1998; VOL 23; NUMB 5; SUPP 1 P: SA399

Elsevier Science, 1998

ISSN: 8756-3282

LANGUAGE: English DOCUMENT TYPE: Conference Preprinted abstracts and programme

CONFERENCE SPONSOR: American Society for Bone and Mineral Research International Bone and Mineral Society

CONFERENCE LOCATION: San Francisco, CA

CONFERENCE DATE: Dec 1998 (199812) (199812)

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09/632657

L1 FILE 'REGISTRY' ENTERED AT 15:12:29 ON 18 JUL 2002
43 SEA ABB=ON PLU=ON GCTGATATTCTGGTGGGAAA|GGCAAGAGCAAAACTC
TGTC/SQSN

Seq IDs 7#8

L2 FILE 'HCAPLUS' ENTERED AT 15:17:30 ON 18 JUL 2002
10 SEA ABB=ON PLU=ON L1

L2 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:290495 HCAPLUS
Correction of: 2001:186025
DOCUMENT NUMBER: 134:350281
Correction of: 134:234030
TITLE: Gene expression marker nucleic acids and
proteins for identification, assessment,
prevention, and therapy of ovarian cancer
INVENTOR(S): Lee, John; Thompsho, Pamela; Lillie, James
PATENT ASSIGNEE(S): Millennium Predictive Medicine, Inc., USA
SOURCE: PCT Int. Appl., 1198 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018542	A2	20010315	WO 2000-US24199	20000901
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG				
PRIORITY APPLN. INFO.:				
US 1999-PV152547 19990903				
US 2000-PV190347 20000316				
US 2000-PV191321 20000321				
US 2000-PV208382 20000531				
US 2000-PV220467 20000720				

AB The invention relates to compns., kits, and methods for detecting, characterizing, preventing, and treating human ovarian cancers. A variety of markers are provided, wherein changes in the levels of expression of one or more of the markers is correlated with the presence of ovarian cancer. The level of expression of the marker in a sample can be assessed, for example, by detecting the presence in the sample of: (1) a protein corresponding to the marker or a fragment of the protein using a reagent, such as an antibody or antibody deriv. or fragment, which binds specifically with the protein; (2) a transcribed polynucleotide (e.g., an mRNA or cDNA) having at least a portion with which the marker is substantially homologous by contacting a mixt. of transcribed polynucleotides obtained from the sample with a substrate having one or more of the markers provided; (3) a transcribed polynucleotide, wherein the polynucleotide anneals with the marker under stringent hybridization conditions. [This abstr. record is the second of five records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

IT 202498-11-1, GenBank AC004000

Searcher : Shears 308-4994

09/632657

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(nucleotide sequence; gene expression marker nucleic acids and
proteins for identification, assessment, prevention, and therapy
of ovarian cancer)

L2 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:168192 HCAPLUS

DOCUMENT NUMBER: 134:217981

TITLE: Genetic techniques for determining genotype of
IL-1 gene cluster (IL-1A, IL-1B and IL-1RN
genes) in females, and their use in determining
susceptibility of female to developing
osteoporosis

INVENTOR(S): Van Dijk, Simon; Duff, Gordon W.

PATENT ASSIGNEE(S): Interleukin Genetics, Inc., USA

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016377	A2	20010308	WO 2000-US23844	20000830
WO 2001016377	A3	20020117		
W:	AE, AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, TR, US, YU, ZA			
RW:	AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
BR 2000014150	A	20020514	BR 2000-14150	20000830
EP 1212464	A2	20020612	EP 2000-961425	20000830
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY			

PRIORITY APPLN. INFO.:

US 1999-151460P P 19990830

WO 2000-US23844 W 20000830

AB The invention provides mol. genetic techniques for detg. the genotype of the IL-1 gene cluster (IL-1A, IL-1B and IL-1RN genes) in females, in order to det. the susceptibility of a female to developing osteoporosis. The invention relates that gene IL-1A encodes interleukin 1.alpha., gene IL-1B encodes interleukin 1.beta., while gene IL-1RN encodes interleukin 1 receptor antagonist. The invention provides that the IL-1A, IL-1B and IL-1RN alleles can be detecting using: (1) allele-specific hybridization; (2) DNA sequencing of a portion of the allele; (3) electrophoresis mobility of allele or fragments generated using a restriction endonuclease; (4) single-stranded conformation polymorphism; (5) oligonucleotide ligation assay, or (6) primer specific extension. The invention also relates that the alleles may be subjected to an amplification step prior to the detection steps listed above. The invention further relates that females contg. allele 2 of IL-1A, allele 2 of IL-1B (3954), allele 1 of IL-1B (-511), and allele 1 of IL-1RN (haplotype 1) are susceptible to larger bone loss and/or increased risk of fractures during the early menopausal years. Still further, the invention relates that females contg. allele 1 of IL-1A, allele 1 of IL-1B (3954), allele 2 of IL-1B (-511) and allele 2 of IL-1RN (haplotype 2) are susceptible to larger bone loss and/or

Searcher : Shears 308-4994

09/632657

increased risk of fractures during post-menopause. The invention also provides a method for screening test compds. to identify therapeutics for osteoporosis, wherein the therapeutics are modulators (antagonists or agonists) of IL-1 activity. The invention further provides for the use of identified therapeutic in treatment and/or prevention of osteoporosis. Finally, the invention provides a method for detg. the effectiveness of therapeutic in a subject who has or is predisposed to developing osteoporosis.

IT 244295-41-8 244295-42-9

RL: PRP (Properties)

(unclaimed sequence; genetic techniques for detg. genotype of IL-1 gene cluster (IL-1A, IL-1B and IL-1RN genes) in females, and their use in detg. susceptibility of female to developing osteoporosis)

L2 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:12669 HCAPLUS

DOCUMENT NUMBER: 134:85136

TITLE: Diagnostics and therapeutics for diseases associated with an IL-1 inflammatory haplotype
INVENTOR(S): Duff, Gordon W.; Cox, Angela; Camp, Nicola Jane; Di, Giovine Francesco Saverio

PATENT ASSIGNEE(S): Interleukin Genetics, Inc., USA

SOURCE: PCT Int. Appl., 84 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000880	A2	20010104	WO 2000-US18318	20000630
WO 2001000880	A3	20011115		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6268142	B1	20010731	US 1999-345217	19990630
EP 1194590	A2	20020410	EP 2000-947005	20000630
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

PRIORITY APPLN. INFO.:
US 1999-345217 A 19990630
GB 1997-11040 A 19970529
WO 1998-GB1481 A1 19980521
WO 2000-US18318 W 20000630

AB Methods and kits for detg. whether a subject has or is predisposed to developing a disease which is assocd. with IL-1 polymorphisms and assays for identifying therapeutics for treating and/or preventing the development of these diseases are provided. The disease of condition is selected from inflammatory disease, degenerative disease, immunol. disease, infectious disease, trauma induced disease, and cancer.

Searcher : Shears 308-4994

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IT 244295-41-8 244295-42-9

RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (diagnostics and therapeutics for diseases assocd. with an IL-1 inflammatory haplotype)

L2 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:842372 HCAPLUS

DOCUMENT NUMBER: 134:14046

TITLE: Diagnostics and therapeutics for cardiovascular disorders based on genotyping of the interleukin-1 family

INVENTOR(S): Francis, Sheila E.; Crossman, David C.; Duff, Gordon W.; Kornman, Kenneth S.

PATENT ASSIGNEE(S): Interleukin Genetics, Inc., USA

SOURCE: PCT Int. Appl., 122 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072015	A2	20001130	WO 2000-US14775	20000526
WO 2000072015	A3	20020207		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1192279	A2	20020403	EP 2000-939389	20000526
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

PRIORITY APPLN. INFO.: US 1999-320395 A 19990526
US 1999-431352 A 19991101
WO 2000-US14775 W 20000526

AB The kits and methods of the present invention relate to the diagnosis of cardiovascular disorders, ie., either a fragile plaque disorder, an occlusive disorder, or a restenosis disorder. Polymorphisms of the interleukin-1 gene family assocd. with cardiovascular disorders are identified as IL-1A(+4845), IL-1B(+3954), IL-1B(-511), IL-1RN(+2018), and alleles in linkage disequil. with these aforementioned alleles. Thus, predispositions toward cardiovascular disorders can be diagnosed by genotyping techniques such as size anal. of DNA fragments after restriction enzyme digestion. IL-1 genotypes are also correlated with target vessel revascularization, cholesterol levels, Lp(a) levels, LDL levels, and C-reactive protein levels. Other methods of the present invention relate to the selection of therapeutics for a patient with a cardiovascular disease.

IT 244295-41-8 244295-42-9

RL: PRP (Properties)

09/632657

(unclaimed nucleotide sequence; diagnostics and therapeutics for cardiovascular disorders based on genotyping of the interleukin-1 family)

L2 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:842310 HCAPLUS
DOCUMENT NUMBER: 134:26093
TITLE: Diagnostics and therapeutics for restenosis
based on genotyping of the interleukin-1 family
INVENTOR(S): Kornman, Kenneth S.; Duff, Gordon W.; Crossman,
David C.; Francis, Sheila E.; Stephenson,
Katherine
PATENT ASSIGNEE(S): Interleukin Genetics, Inc., USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071753	A2	20001130	WO 2000-US14299	20000524
WO 2000071753	A3	20020207		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1192277	A2	20020403	EP 2000-937731	20000524
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

PRIORITY APPLN. INFO.:
US 1999-317674 A 19990524
US 1999-431352 A 19991101
WO 2000-US14299 W 20000524

AB Methods and kits for detg. whether a subject has or is predisposed to developing restenosis are provided. Polymorphisms of the interleukin-1 (IL-1) family assocd. with restenosis are identified as IL-1A(+4845), IL-1B(+3954), IL-1B(-511), IL-1RN(+2018), and IL-1RN(VNTR) or an allele that is in linkage disequil. with one of these alleles. Thus, predisposition to arterial restenosis can be diagnosed by genotyping techniques, such as size anal. of DNA fragments after restriction enzyme digestion. Such patients might be preferred candidates for surgical revascularization rather than percutaneous transluminal angioplasty, for example, or such patients may benefit from pharmacol. or topical interventions at an early stage that could affect the progression of the restenosis disorder.

IT 244295-41-8 244295-42-9

RL: PRP (Properties)

(unclaimed nucleotide sequence; diagnostics and therapeutics for restenosis based on genotyping of the interleukin-1 family)

L2 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:725801 HCAPLUS

Searcher : Shears 308-4994

09/632657

DOCUMENT NUMBER: 133:294920
TITLE: Genetic markers for use in assessing the risk of
interstitial lung disease
INVENTOR(S): Duff, Gordon W.; Di Giovine, Francesco Saverio;
Whyte, Moria
PATENT ASSIGNEE(S): Interleukin Genetics, Inc., USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000060117	A2	20001012	WO 2000-US8492	20000331
WO 2000060117	A3	20020207		
W:	AE, AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, TR, US, YU, ZA			
RW:	AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
EP 1192275	A2	20020403	EP 2000-921536	20000331
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			

PRIORITY APPLN. INFO.: US 1999-286108 A 19990402
WO 2000-US8492 W 20000331

AB The present invention provides novel methods and kits for detg. whether a subject has or is likely to develop an interstitial lung disorder such as pulmonary fibrosis; as well as methods for treating an ILD and screening assays for identifying novel ILD therapeutics. The method uses polymorphisms in the interleukin 1 gene cluster on 2q13 and the tumor necrosis factor region on chromosome 6 as indicators of risk.

IT 244295-41-8 244295-42-9

RL: PRP (Properties)
(unclaimed nucleotide sequence; genetic markers for use in assessing the risk of interstitial lung disease)

L2 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:441964 HCAPLUS
DOCUMENT NUMBER: 133:85082
TITLE: Diagnostic and therapeutics for sepsis by
studying interleukin 1 gene polymorphism
INVENTOR(S): Di Giovine, Francesco S.; Duff, Gordon W.
PATENT ASSIGNEE(S): Interleukin Genetics, Inc., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037679	A2	20000629	WO 1999-US25633	19991101
WO 2000037679	A3	20010111		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,			

Searcher : Shears 308-4994

09/632657

ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 6251598 B1 20010626 US 1998-183850 19981030
EP 1127168 A2 20010829 EP 1999-972008 19991101
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
PT, IE, SI, LT, LV, FI, RO
US 2001034032 A1 20011025 US 2001-852948 20010510
PRIORITY APPLN. INFO.: US 1998-183850 A 19981030
WO 1999-US25633 W 19991101

AB Methods and kits for detecting polymorphism that are predictive of a subject's susceptibility to developing sepsis are described and sepsis therapeutics that address the mol. basis of the disease are described. The invention is based on detg. at least one allele of the interleukin 1 (IL-1) genetic pattern that leads to a dysregulated inflammatory response. In a further aspect, the invention features methods for treating or preventing the development of sepsis by administering an appropriate therapeutic of the invention.

IT 244295-41-8 244295-42-9

RL: PRP (Properties)

(unclaimed nucleotide sequence; diagnostic and therapeutics for sepsis by studying interleukin 1 gene polymorphism)

L2 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:366621 HCAPLUS

DOCUMENT NUMBER: 132:344010

TITLE: The DNA sequence of human chromosome 21

AUTHOR(S): Hattori, M.; Fujiyama, A.; Taylor, T. D.;
Watanabe, H.; Yada, T.; Park, H.-S.; Toyoda, A.;
Ishil, K.; Totoki, Y.; Choi, D.-K.; Soeda, E.;
Ohki, M.; Takagi, T.; Sakaki, Y.; Taudlen, S.;
Blechs Schmidt, K.; Polley, A.; Menzel, U.;
Delabar, J.; Kumpf, K.; Lehmann, R.; Patterson,
D.; Reichwald, K.; Rump, A.; Schillhabel, M.;
Schudy, A.; Zimmermann, W.; Rosenthal, A.;
Kudoh, J.; Shibuya, K.; Kawasaki, K.; Asakawa,
S.; Shintani, A.; Sasaki, T.; Nagamine, K.;
Mitsuyama, S.; Antonarakis, S. E.; Minoshima,
S.; Shimizu, N.; Nordsiek, G.; Hornischer, K.;
Brandt, P.; Scharfe, M.; Schon, O.; Desario, A.;
Relchelt, J.; Kauer, G.; Blocker, H.; Ramser,
J.; Beck, A.; Klages, S.; Hennig, S.;
Riesseltmann, L.; Dagand, E.; Haaf, T.;
Wehrmeyer, S.; Borzym, K.; Gardiner, K.;
Nizetic, D.; Francis, F.; Lehrach, H.;
Reinhardt, R.; Yaspo, M.-L.

CORPORATE SOURCE: Genomic Sciences Center, RIKEN, Sagamihara,
228-8555, Japan

SOURCE: Nature (London) (2000), 405(6784), 311-319
CODEN: NATUAS; ISSN: 0028-0836

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

Searcher : Shears 308-4994

09/632657

AB Chromosome 21 is the smallest human autosome. An extra copy of chromosome 21 causes Down syndrome, the most frequent genetic cause of significant mental retardation, which affects up to 1 in 700 live births. Several anonymous loci for monogenic disorders and predispositions for common complex disorders have also been mapped to this chromosome, and loss of heterozygosity has been obsd. in regions assocd. with solid tumors. This report provides the sequence and gene catalog of the long arm of chromosome 21. At least 33,546,361 base pairs (bp) of DNA have been sequenced with very high accuracy, the largest contig being 25,491,867 bp. Only 3 small clone gaps and 7 sequencing gaps remain, comprising .apprx.100 kilobases. Thus, 99.7% coverage of 21q was achieved. About 281,116 bp were also sequenced from the short arm. The structural features identified include duplications that are probably involved in chromosomal abnormalities and repeat structures in the telomeric and pericentromeric regions. Anal. of the chromosome revealed 127 known genes, 98 predicted genes and 59 pseudogenes. The sequences are deposited in the GenBank database, and addnl. information can be found from the home pages of the participating centers of the chromosome 21 sequencing consortium.

IT 264819-19-4, GenBank AL163215

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(nucleotide sequence; DNA sequence of human chromosome 21)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:691285 HCAPLUS

DOCUMENT NUMBER: 131:318551

TITLE: Fetal testing for prediction of low birth weight using PCR genotyping

INVENTOR(S): Kornman, Kenneth S.; Offenbacher, Steven; Duff, Gordon W.

PATENT ASSIGNEE(S): Medical Science Systems, Inc., USA

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954707	A2	19991028	WO 1999-US8794	19990421
WO 9954707	A3	20000622		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2328955	AA	19991028	CA 1999-2328955	19990421
AU 9937557	A1	19991108	AU 1999-37557	19990421

Searcher : Shears 308-4994

09/632657

EP 1071822 A2 20010131 EP 1999-919959 19990421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
PT, IE, FI
JP 2002512047 T2 20020423 JP 2000-545003 19990421
PRIORITY APPLN. INFO.: US 1998-82487P P 19980421
WO 1999-US8794 W 19990421

AB Methods, assays and kits are disclosed for detecting a mother's or a fetus's susceptibility to an adverse pregnancy outcome such as low birth wt. The methods comprise obtaining a biol. sample from a patient and detg. the presence or absence of an IL-1 allele 2 of a marker that is assocd. with an adverse pregnancy outcome. Alleles for TNF.alpha. and Prostaglandin E2 were also genotyped. Detection of alleles by VNTR polymorphism and and PCR RFLP is described. Diagrams showing relationship between maternal urogenital or periodontal infection and fetal inflammatory response and maternal infection and inflammatory cytokines and risk of adverse pregnancy outcome. Genotype anal. was performed and characterized according to race from samples of maternal blood and chorionic villus and umbilical cord.

IT 244295-41-8 244295-42-9
RL: PRP (Properties)
(unclaimed nucleotide sequence; fetal testing for prediction of low birth wt. using PCR genotyping)

L2 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:641021 HCAPLUS

DOCUMENT NUMBER: 131:253337

TITLE: Methods and materials for the diagnosis of asthma wherein the genetic polymorphism D2S308*3 is the subject of detection

INVENTOR(S): Cookson, William Osmond Charles Michael;
Moffatt, Miriam Fleur; Bhattacharyya, Sumit;
Leaves, Nicholas

PATENT ASSIGNEE(S): Isis Innovation Ltd., UK

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9950451	A1	19991007	WO 1999-GB968	19990326
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9931587	A1	19991018	AU 1999-31587	19990326
EP 1064401	A1	20010103	EP 1999-913469	19990326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1998-6652 A 19980327
WO 1999-GB968 W 19990326

AB A genetic method for diagnosing an individual as being asthmatic, or as having a predisposition to asthma, is described. The materials and methods of the invention are used to detect the presence or absence of the genetic polymorphism known as D2S308*3, which is located in a region of chromosome 2. The invention provides

Searcher : Shears 308-4994

09/632657

oligonucleotide primers for use in detecting said polymorphism. The allele of identification may take the form of microsatellite repeats, and thus, oligonucleotide primers which hybridize to sequences at positions on either side of the microsatellite repeats are provided herein.

IT 244295-41-8 244295-42-9

RL: PRP (Properties)

(unclaimed sequence; methods and materials for the diagnosis of asthma wherein the genetic polymorphism D2S308*3 is the subject of detection)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

E1 THROUGH E4 ASSIGNED

FILE 'REGISTRY' ENTERED AT 15:18:39 ON 18 JUL 2002

L3 4 SEA FILE=REGISTRY ABB=ON PLU=ON (244295-41-8/BI OR 244295-42-9/BI OR 202498-11-1/BI OR 264819-19-4/BI)

L3 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2002 ACS

RN 264819-19-4 REGISTRY

CN DNA (human clone R396A17 chromosome 21 segment HS21C015) (9CI) (CA INDEX NAME)

SQL 340000

MF Unspecified

CI MAN

REFERENCE 1: 132:344010

L3 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2002 ACS

RN 244295-42-9 REGISTRY

CN PN: WO9950451 SEQID: 10 unclaimed sequence (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 14: PN: WO0037679 SEQID: 14 unclaimed DNA

CN 14: PN: WO0072015 SEQID: 17 unclaimed DNA

CN 18: PN: WO0071753 SEQID: 21 unclaimed DNA

CN 2: PN: WO0116377 PAGE: 22 unclaimed sequence

CN 4: PN: WO0060117 PAGE: 40 unclaimed DNA

CN 4: PN: WO0100880 SEQID: 7 claimed DNA

CN PN: WO9954707 SEQID: 22 unclaimed DNA

SQL 20 ← Seq. displayed @ L4 (2-4)

MF Unspecified

CI MAN

REFERENCE 1: 134:217981

REFERENCE 2: 134:85136

REFERENCE 3: 134:26093

REFERENCE 4: 134:14046

REFERENCE 5: 133:294920

REFERENCE 6: 133:85082

REFERENCE 7: 131:318551

Searcher : Shears 308-4994

09/632657

REFERENCE 8: 131:253337

L3 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2002 ACS

RN 244295-41-8 REGISTRY

CN PN: WO9950451 SEQID: 9 unclaimed sequence (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 13: PN: WO0037679 SEQID: 13 unclaimed DNA

CN 13: PN: WO0072015 SEQID: 16 unclaimed DNA

CN 17: PN: WO0071753 SEQID: 20 unclaimed DNA

CN 1: PN: WO0116377 PAGE: 22 unclaimed sequence

CN 3: PN: WO0060117 PAGE: 40 unclaimed DNA

CN 3: PN: WO0100880 SEQID: 6 claimed DNA

CN PN: WO9954707 SEQID: 21 unclaimed DNA

SQL 20 ← Seq. displayed CL4 (3-4)

MF Unspecified

CI MAN

REFERENCE 1: 134:217981

REFERENCE 2: 134:85136

REFERENCE 3: 134:26093

REFERENCE 4: 134:14046

REFERENCE 5: 133:294920

REFERENCE 6: 133:85082

REFERENCE 7: 131:318551

REFERENCE 8: 131:253337

L3 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2002 ACS

RN 202498-11-1 REGISTRY

CN DNA (human clone WO0118542_SEQID_3147 ovary tumor-associated protein cDNA) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN PN: WO0118542 SEQID: 3147 claimed DNA

SQL 128117

MF Unspecified

CI MAN

REFERENCE 1: 134:350281

L4 4 S L3 AND L1

L4 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2002 ACS

RN 244295-42-9 REGISTRY

CN PN: WO9950451 SEQID: 10 unclaimed sequence (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 14: PN: WO0037679 SEQID: 14 unclaimed DNA

CN 14: PN: WO0072015 SEQID: 17 unclaimed DNA

CN 18: PN: WO0071753 SEQID: 21 unclaimed DNA

CN 2: PN: WO0116377 PAGE: 22 unclaimed sequence

Searcher : Shears 308-4994

09/632657

CN 4: PN: WO0060117 PAGE: 40 unclaimed DNA
CN 4: PN: WO0100880 SEQID: 7 claimed DNA
CN PN: WO9954707 SEQID: 22 unclaimed DNA
CI MAN

SQL 20

SEQ 1 ggcaagagca aaactctgtc
=====

HITS AT: 1-20

REFERENCE 1: 134:217981

REFERENCE 2: 134:85136

REFERENCE 3: 134:26093

REFERENCE 4: 134:14046

REFERENCE 5: 133:294920

REFERENCE 6: 133:85082

REFERENCE 7: 131:318551

REFERENCE 8: 131:253337

L4 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 244295-41-8 REGISTRY
CN PN: WO9950451 SEQID: 9 unclaimed sequence (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 13: PN: WO0037679 SEQID: 13 unclaimed DNA
CN 13: PN: WO0072015 SEQID: 16 unclaimed DNA
CN 17: PN: WO0071753 SEQID: 20 unclaimed DNA
CN 1: PN: WO0116377 PAGE: 22 unclaimed sequence
CN 3: PN: WO0060117 PAGE: 40 unclaimed DNA
CN 3: PN: WO0100880 SEQID: 6 claimed DNA
CN PN: WO9954707 SEQID: 21 unclaimed DNA
CI MAN

SQL 20

SEQ 1 gctgatattc tgggtgggaaa
=====

HITS AT: 1-20

REFERENCE 1: 134:217981

REFERENCE 2: 134:85136

REFERENCE 3: 134:26093

REFERENCE 4: 134:14046

REFERENCE 5: 133:294920

REFERENCE 6: 133:85082

REFERENCE 7: 131:318551

09/632657

REFERENCE 8: 131:253337

=> e interleukin 1a/cn 5

E1 1 INTERLEUKIN 19 (HUMAN PRECURSOR)/CN
E2 1 INTERLEUKIN 19 (HUMAN)/CN
E3 0 --> INTERLEUKIN 1A/CN
E4 1 INTERLEUKIN 1H (HUMAN LONG ISOFORM A PRECURSOR)/CN
E5 1 INTERLEUKIN 1H (HUMAN LONG ISOFORM PRECURSOR)/CN

-key terms

=> e "interleukin-1a"/cn 5

E1 1 INTERLEUKIN-18 RECEPTOR (HUMAN SUBUNIT ACPL)/CN
E2 1 INTERLEUKIN-18 RECEPTOR (HUMAN SUBUNIT IL-1RRP1)/CN
E3 0 --> INTERLEUKIN-1A/CN
E4 2 INTERLEUKIN-1B CONVERTING ENZYME (HUMAN ISOLATE 1 YEAR
OLD MALE CELL LINE THP.1 - ACUTE MONOCYTIC LEUKEMIA)
/CN
E5 1 INTERLEUKIN-1H1 (HUMAN KERATINOCYTE)/CN

=> s e4

L5 2 "INTERLEUKIN-1B CONVERTING ENZYME (HUMAN ISOLATE 1 YEAR
OLD MALE CELL LINE THP.1 - ACUTE MONOCYTIC LEUKEMIA)"/CN

=> e interleukin 1rn/cn 5

E1 2 INTERLEUKIN 1H4 (HUMAN)/CN
E2 1 INTERLEUKIN 1HY2 (HUMAN SKIN GENE IL1HY2)/CN
E3 0 --> INTERLEUKIN 1RN/CN
E4 1 INTERLEUKIN 2 (107-THREONINE) (HUMAN)/CN
E5 1 INTERLEUKIN 2 (107-THREONINE,125-SERINE) (HUMAN)/CN

=> e "interleukin-1rn"/cn 5

E1 1 INTERLEUKIN-1H4 (HUMAN LUNG PRECURSOR)/CN
E2 1 INTERLEUKIN-1RA (DOG MONONUCLEAR CELL PRECURSOR)/CN
E3 0 --> INTERLEUKIN-1RN/CN
E4 1 INTERLEUKIN-2 (GUINEA PIG SPLENOCYTE PRECURSOR)/CN
E5 1 INTERLEUKIN-2 (HUMAN CLONE PILOT135-8)/CN

=> e il 1a/cn 5

E1 1 IL 11/CN
E2 1 IL 16/CN
E3 0 --> IL 1A/CN
E4 1 IL 2/CN
E5 1 IL 2066/CN

=> e "il-1a"/cn 5

E1 1 IL-17B RECEPTOR (HUMAN GENE IL17BR)/CN
E2 1 IL-19 (HUMAN CLONE HMQB23 PRECURSOR)/CN
E3 0 --> IL-1A/CN
E4 1 IL-1RRP2 (HUMAN)/CN
E5 1 IL-1RRP2 (MOUSE)/CN

=> e "interleukin-1-.alpha." /cn 5

E1 1 INTERLEUKIN-1 RECEPTOR-TUMOR NECROSIS FACTOR RECEPTOR-
TUMOR NECROSIS FACTOR RECEPTOR FUSION PROTEIN (HUMAN)/
CN
E2 1 INTERLEUKIN-1 TYPE I RECEPTOR KINASE/CN
E3 0 --> INTERLEUKIN-1-.ALPHA./CN
E4 1 INTERLEUKIN-1-LIKE PROTEIN 1 (HUMAN CLONE PAC-131J6 GE

09/632657

E5 1 NE IL1L1)/CN
INTERLEUKIN-1-LIKE PROTEIN 1 (HUMAN PLACENTA GENE IL1L
1 TRANSCRIPT 2)/CN

=> e "interleukin 1-.alpha."/cn 5

E1 1 INTERLEUKIN 1 RECEPTOR-RELATED PROTEIN IL1-RRP1 (HUMAN
PRECURSOR)/CN
E2 1 INTERLEUKIN 1 RECEPTOR-RELATED PROTEIN IL1-RRP1 (MOUSE
PRECURSOR)/CN
E3 0 --> INTERLEUKIN 1-.ALPHA./CN
E4 1 INTERLEUKIN 1-BETA CONVERTASE (HUMAN GENE IL1BCE)/CN
E5 1 INTERLEUKIN 1-BETA CONVERTING ENZYME ISOFORM DELTA (HU
MAN CELL LINE THP-1 CLONE ICE-DELTA GENE IL1BCE)/CN

=> e "interleukin 1-alpha"/cn 5

E1 1 INTERLEUKIN 1 RECEPTOR-RELATED PROTEIN IL1-RRP1 (HUMAN
PRECURSOR)/CN
E2 1 INTERLEUKIN 1 RECEPTOR-RELATED PROTEIN IL1-RRP1 (MOUSE
PRECURSOR)/CN
E3 0 --> INTERLEUKIN 1-ALPHA/CN
E4 1 INTERLEUKIN 1-BETA CONVERTASE (HUMAN GENE IL1BCE)/CN
E5 1 INTERLEUKIN 1-BETA CONVERTING ENZYME ISOFORM DELTA (HU
MAN CELL LINE THP-1 CLONE ICE-DELTA GENE IL1BCE)/CN

=> e "interleukin 1alpha"/cn 5

E1 1 INTERLEUKIN 19 (HUMAN PRECURSOR)/CN
E2 1 INTERLEUKIN 19 (HUMAN)/CN
E3 0 --> INTERLEUKIN 1ALPHA/CN
E4 1 INTERLEUKIN 1H (HUMAN LONG ISOFORM A PRECURSOR)/CN
E5 1 INTERLEUKIN 1H (HUMAN LONG ISOFORM PRECURSOR)/CN

=> e interleukin 1/cn 5

E1 1 INTERLEUKIN (DOG STRAIN BEAGLE GENE IL-10 PRECURSOR)/C
N
E2 1 INTERLEUKIN (HUMAN CLONE PIL-1-14 REDUCED), N-L-METHIO
NYL-35-L-ASPARAGINE-/CN
E3 0 --> INTERLEUKIN 1/CN
E4 1 INTERLEUKIN 1 (FLOUNDER CLONE PSR.ALPHA.-IL2 PRECURSOR
REDUCED)/CN
E5 1 INTERLEUKIN 1 (FLOUNDER CLONE PSR.ALPHA.-IL2 REDUCED)/
CN

=> s interleukin 1 ?/cn

L6 101 INTERLEUKIN 1 ?/CN

=> s "interleukin-1"?/cn

L7 126 "INTERLEUKIN-1"?/CN

=> s 15 or 16 or 17

L8 216 L5 OR L6 OR L7

FILE 'HCAPLUS' ENTERED AT 15:26:50 ON 18 JUL 2002

L9 39088 SEA ABB=ON PLU=ON L8 OR (INTERLEUKIN OR IL) (W) (1A OR 1
OR 1B OR 1A OR 1B OR 1RN OR 1RN) OR IL1A OR IL1B OR IL1A
L10 67 SEA ABB=ON PLU=ON L9 AND (PREMENOPAUS? OR PERIMENOPAUS?
OR MENOPAUS? OR "CHANGE OF LIFE")
L11 4 SEA ABB=ON PLU=ON L10 AND (MUTAT? OR MUTANT OR
MUTAGEN? OR POLYMORPH? OR POLY MORPH? OR (VARIAT? OR

Searcher : Shears 308-4994

09/632657

VARIANT) (5A) ALLEL?)

L12 3 SEA ABB=ON PLU=ON L11 NOT L2

L12 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:517497 HCAPLUS

DOCUMENT NUMBER: 134:99462

TITLE: Linkage of human tumor necrosis factor-alpha to human osteoporosis by sib-pair analysis

AUTHOR(S): Ota, N.; Hunt, S. C.; Nakajima, T.; Suzuki, T.; Hosoi, T.; Orimo, H.; Shirai, Y.; Emi, M.

CORPORATE SOURCE: Department of Molecular Biology, Institute of Gerontology, Nippon Medical School, Kawasaki, 211-8533, Japan

SOURCE: Genes and Immunity (2000), 1(4), 260-264

CODEN: GEIMA2; ISSN: 1466-4879

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteoporosis as well as osteopenia are common human conditions considered to result from the interplay of multiple genetic and environmental factors. Twin and family studies have yielded strong correlation between measures of bone mass and a no. of genetic factors. Certain genes (e.g., cytokines such as **interleukin-1**, interleukin-6, or tumor necrosis factor-alpha) are capable of regulating metab., formation, and resorption of bone; all processes that det. bone mass. We tested 192 sib-pairs of adult Japanese women from 136 families for genetic linkage between osteoporosis and osteopenia phenotypes and **allelic variants** at the tumor necrosis factor-alpha (TNFA) locus, using a dinucleotide-repeat **polymorphism** located near the gene. The TNFA locus showed evidence for linkage to osteoporosis, with mean allele sharing of 0.478 in discordant pairs and 0.637 in concordant affected pairs. Linkage with osteopenia was also significant in concordant affected pairs. Analyses limited to the post-menopausal women in our cohort showed similar or even stronger linkage for both phenotypes. The results provide evidence that genetic variations within the TNFA locus or adjacent genes affect regulation of mineral metab. in bone and some of them confer risk for osteoporosis in adult women.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:653159 HCAPLUS

DOCUMENT NUMBER: 130:65022

TITLE: **Allelic variation** at the **interleukin-1** receptor

antagonist gene is associated with early postmenopausal bone loss at the spine

AUTHOR(S): Keen, R. W.; Woodford-Richens, K. L.; Lanchbury, J. S.; Spector, T. D.

CORPORATE SOURCE: Twin & Genetic Epidemiology Research Unit, St. Thomas' Hospital, London, UK

SOURCE: Bone (New York) (1998), 23(4), 367-371

CODEN: BONEDL; ISSN: 8756-3282

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

Searcher : Shears 308-4994

09/632657

LANGUAGE: English

AB Genetic factors play an important role in detg. bone mineral d. (BMD) in later life, with the genetic influence mediated through effects on both peak mass and on age- and **menopause**-related bone loss. At **menopause** there is an increase in the prodn. and activity of various cytokines and growth factors within the bone microenvironment. The activity of **interleukin-1 (IL-1)**, a powerful stimulant of osteoclastic bone resorption, is increased in estrogen-deficient states with increased prodn. of **IL-1** and inhibition of the **IL-1** receptor antagonist (**IL-1ra**). Treatment with **IL-1ra** blocks the bone loss assocd. with ovariectomy in animals and the **IL-1** receptor antagonist gene (**IL-1RN**) is therefore a potential candidate gene for the regulation of postmenopausal bone loss. We examd. the relationship between annual rates of change in BMD over 5 yr and an 86 bp variable no. tandem-repeat **polymorphism** of the **IL-1RN** gene in 108 early postmenopausal women. All women were within 5 yr of a natural **menopause** at the study's onset, healthy, and not on hormone replacement therapy or other medication known to affect bone metab. BMD was measured annually over the 5 yr study period at the lumbar spine and femoral neck using dual-energy x-ray absorptiometry. Three alleles were identified (A1=4 repeats, A2=2 repeats, A3=5 repeats), with five genotypes obsd.: A1A1 (41.7%), A1A2 (45.4%), A2A2 (6.5%), A1A3 (2.8%), and A2A3 (3.7%). For anal., alleles were collapsed into a biallelic system grouping the A1 and A3 alleles. There was no significant relationship between the **IL-1RN** genotypes and baseline bone mass at either the spine or hip. **IL-1RN** genotype was significantly assocd. with annual rates of change in spinal bone mass ($p < 0.05$), and this finding remained significant after adjustment for age, wt., and baseline BMD. Carriage of at least one copy of the A2 allele was assocd. with reduced bone loss at the spine (mean change in BMD \pm SD: $-0.81 \pm 1.46\%/yr$) when compared with noncarriage of the A2 allele (mean change $-1.38 \pm 1.48\%/yr$), $p = 0.05$. We therefore conclude that **allelic variation** at the **IL-1RN** locus is assocd. with differential rates of early postmenopausal bone loss at the spine. Further research will be required to clarify the mechanisms underlying these findings and to det. whether this assocn. translates into a significant long-term effect on BMD and fracture in later life.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:556335 HCAPLUS

DOCUMENT NUMBER: 127:229687

TITLE: Changes of bone metabolism with aging - in relation to involvement of estrogen withdrawal

AUTHOR(S): Gorai, Itsuo

CORPORATE SOURCE: Dep. Obstetrics Gynecol., Yokohama City Univ. Sch. Med., Yokohama, Japan

SOURCE: Nippon Sanka Fujinka Gakkai Zasshi (1997), 49(8), 537-545, 563-576

CODEN: NISFAY; ISSN: 0300-9165

PUBLISHER: Nippon Sanka Fujinka Gakkai

Searcher : Shears 308-4994

DOCUMENT TYPE: Journal; General Review
 LANGUAGE: Japanese

AB A review and discussion with no refs. The diminution of bone mineral d. (BMD) in women is initiated at the onset of **menopause** and estrogen withdrawal causes rapid bone loss in early postmenopausal years, leading to an increase in a risk of osteoporotic fracture. Several cytokines are considered to be involved in the decrease of BMD due to estrogen deficiency. Recently, it has been reported that estrogen is important for bone maturation and mineralization in men as well as in women. In this study, we investigated the involvement of estrogen deficiency in bone metab. of postmenopausal women as compared with **premenopausal** women and assessed the factors relating to postmenopausal bone loss. In exptl. study, at 4 wk after ovariectomy (OVX), in OVX mice, femoral BMD decreased whereas the no. of bone marrow cells was greatly increased. To explore the endogenous bone-resorbing factors involved in estrogen deficiency, we examd. the bone-resorbing activity in the supernatant fraction of mouse bone marrow collected from ovariectomized mice. Only anti-interleukin (IL)-1a antibody completely neutralized the bone-resorbing activity in bone marrow supernatants from OVX mice. The concurrent addn. of IL-1, IL-6 sIL-6 receptor (R) and prostaglandin (PG)E2 co-operatively induced bone resorption. The effect of L-1a on collagenase and gelatinase activities and matrix metalloproteinase (MMP)-2 and MMP-13 mRNA expression was analyzed using IL-1a supplemented medium of organ culture of newborn mouse calvaria and osteoblasts from newborn mouse calvaria, resp. IL-1a increased collagenase and gelatinase activities as compared with those of control medium and stimulated MMP-2 and MMP-13 mRNA expression. Human osteoblast-like cells, HOS TE 85 cells, showed aromatase activity, which was detd. using 3H-androstenedione as a substrate and addn. of retinoic acid. TPA, bone morphogenic protein (BMP)-2 and dexamethasone increased their aromatase activity. As detd. by RT-PCR method, retinoic acid and TPA increased aromatase mRNA expression of HOS TE 85 cells. At 3 wk after orchidectomy (ORX), in ORX mice, the wt. of seminal vesicles and femoral BMD decreased whereas the no. of bone marrow cells was greatly increased. The change of hemopoiesis and bone metab. induced by ORX were completely restored by the treatment with 1 .mu.g of E2 but not with 10 .mu.g of DHT. In clin. study, several risk factors relating to low bone mass were assessed. Lumbar spine BMD significantly correlated with years since **menopause** (YSM) ($r = -0.366$), body wt. ($r=0.350$), age ($r = -0.340$), body mass index (BMI) ($r=0.242$), and height ($r = 0.212$) in the postmenopausal women. In order to investigate an assocn. between vitamin D receptor (VDR) gene **polymorphism** and BMD or bone loss, we examd. VDR BsmI RFLP with amplification refractory **mutation** system (ARMS) and could not find any significant differences in lumbar spine baseline BMD between the bb genotype and the Bb genotype. In both early and late postmenopausal periods vertebral BMD with the Bb genotype decreased faster than that with the bb genotype ($p=0.001$). When we divided the subjects whose ages were from 45 to 55 yr into two subgroups (pre- and postmenopausal) to assess the effects of **menopause** on biochem. markers of bone resorption, we found a significant 110% increase in cross-linked N-telopeptides of type I collagen (NTx) and a 48% increase in lysylpyridinoline (LP) in post-**menopausal**

09/632657

women compared with age-matched **premenopausal** women. The ROC anal. showed that the cutoff BMD values for discrimination of women with vertebral fracture varied according to the sites and methods of measurement ranging 59.0% of young adult mean value (YAM) of radial trabecular BMD by pQCT to 83.8% of young adult mean value (YAM) of femoral neck BMD by DXA.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:32:47 ON 18 JUL 2002)

L13 18 S L11
L14 14 DUP REM L13 (4 DUPLICATES REMOVED)

L14 ANSWER 1 OF 14 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-010725 [01] WPIDS

DOC. NO. CPI: C2002-002607

TITLE: Detecting **polymorphisms** in the CAG and GGC repeats of the androgen receptor gene which are associated with bone mineral density is useful to determine a predisposition to osteoporosis.

DERWENT CLASS: B04 D16

INVENTOR(S): ROUSSEAU, F

PATENT ASSIGNEE(S): (SIGN-N) SIGNALGENE INC

COUNTRY COUNT: 95

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2001073116	A2	20011004	(200201)*	EN	34
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RW:	AT	BE	CH	CY	DE	DK	EA	ES	FI	FR	GB	GH	GM	GR	IE	IT	KE	LS	LU	MC
	MW	MZ	NL	OA	PT	SD	SE	SL	SZ	TR	TZ	UG	ZW							

W:	AE	AG	AL	AM	AT	AU	AZ	BA	BB	BG	BR	BY	BZ	CA	CH	CN	CO	CR	CU	CZ
	DE	DK	DM	DZ	EE	ES	FI	GB	GD	GE	GH	GM	HR	HU	ID	IL	IN	IS	JP	KE
	KG	KP	KR	KZ	LC	LK	LR	LS	LT	LU	LV	MA	MD	MG	MK	MN	MW	MX	MZ	NO
	NZ	PL	PT	RO	RU	SD	SE	SG	SI	SK	SL	TJ	TM	TR	TT	TZ	UA	UG	US	UZ
	VN	YU	ZA	ZW																

AU 2001044004	A	20011008	(200208)		
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APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001073116	A2	WO 2001-CA402	20010328
AU 2001044004	A	AU 2001-44004	20010328

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001044004	A Based on	WO 200173116

PRIORITY APPLN. INFO: US 2000-192557P 20000328

AN 2002-010725 [01] WPIDS

AB WO 200173116 A UPAB: 20020105

NOVELTY - Determining predisposition to osteoporosis or low or high bone density or turnover comprising determining **polymorphisms** in the CAG and GGC repeats of the androgen receptor (AR) gene, is new.

DETAILED DESCRIPTION - Determining predisposition to

Searcher : Shears 308-4994

09/632657

osteoporosis, low/high bone density/turnover and/or responsiveness to therapy for osteoporosis or prevention of low bone density, comprises determining androgen receptor (AR) **polymorphism** and analyzing **allelic variation** in a sample, where the AR **polymorphism** is (a) a CAG repeat and a GGC repeat **polymorphism**, or (b) an allele in linkage disequilibrium with (a).

INDEPENDENT CLAIMS are also included for the following:

(1) determining predisposition to low/high bone density, comprising determining androgen receptor **polymorphisms** in a sample, where a genotype showing a GGC repeat **polymorphism** associated with a CAG **polymorphism** can be correlated with high/low bone density or turnover;

(2) determining predisposition to androgen hormone-related medical conditions, comprising determining the length of a CAG and/or GGC repeat of the androgen receptor where length of the repeat is indicative of predisposition;

(3) using specific susceptible or resistant AR alleles to set up a screening assay for agents that modulate AR allele-specificity for the purpose preventing low bone density;

(4) selecting AR allele(s) suitable to screen for compounds that modulate AR activity, comprising constructing a recombinant AR comprising the allele(s), assaying function of the recombinant AR and selecting allele(s) that affect AR function;

(5) using combinations of AR **alleles** or their **variant, mutation** or equivalent which show linkage disequilibrium, to screen for agents that modulate AR function for the purpose of increasing bone density or potentiating action of an osteoporosis treatment;

(6) detecting an agent that modulates bone density, comprising contacting the agent with a cell comprising (a) an expression vector comprising a reporter operably linked to a promoter which has an AR response element which affects promoter activity upon binding to androgen, and (b) a combination of AR alleles and assaying the level of the reporter.

USE - The invention is used to determine predisposition to osteoporosis and to find new therapies for the condition.
Dwg.0/1

L14 ANSWER 2 OF 14 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-265896 [27] WPIDS
DOC. NO. CPI: C2001-080455
TITLE: Determining whether a female is predisposed to the developing osteoporosis involves identifying **interleukin-1** haplotype pattern of the female, useful for selecting appropriate osteoporosis therapy .
DERWENT CLASS: B04 D16
INVENTOR(S): DUFF, G; VAN DIJK, S; DUFF, G W
PATENT ASSIGNEE(S): (INTE-N) INTERLEUKIN GENETICS INC
COUNTRY COUNT: 39
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2001016377	A2	20010308	(200127)*	EN	69
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RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AE AU BR CA CN CZ HU IL JP KR MX NO NZ PL RU SG TR US YU ZA

Searcher : Shears 308-4994

09/632657

AU 2000073380 A 20010326 (200137)
EP 1212464 A2 20020612 (200239) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 2000014150 A 20020514 (200240)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001016377	A2	WO 2000-US23844	20000830
AU 2000073380	A	AU 2000-73380	20000830
EP 1212464	A2	EP 2000-961425	20000830
		WO 2000-US23844	20000830
BR 2000014150	A	BR 2000-14150	20000830
		WO 2000-US23844	20000830

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000073380	A Based on	WO 200116377
EP 1212464	A2 Based on	WO 200116377
BR 2000014150	A Based on	WO 200116377

PRIORITY APPLN. INFO: US 1999-151460P 19990830

AN 2001-265896 [27] WPIDS

AB WO 200116377 A UPAB: 20010518

NOVELTY - Determining (I) whether a female is predisposed to developing osteoporosis, involves identifying interleukin (IL)-1 haplotype pattern (HP). Presence of HP 1 or HP 2 indicates that the female is susceptible to larger bone loss and/or increased risk of fracture during the early **menopausal** years (HP1) or post-**menopause** (HP2).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for determining (II) the effectiveness of treating a subject that has or is predisposed to developing osteoporosis with a particular dose of a particular therapeutic comprising:

(a) detecting the level, amount or activity of an IL-1 protein, or an IL-1 mRNA or DNA in a sample obtained from a subject;

(b) administering the particular dose of the particular therapeutic to the subject, detecting the level, amount or activity of an IL-1 protein or an IL-1 mRNA or DNA in a sample obtained from the subject; and

(c) comparing the relative level, amount or activity of an IL-1 protein obtained before and after the administration of the therapeutic.

USE - The method is useful for determining whether a female is predisposed to developing osteoporosis. (I) is useful for selecting an appropriate osteoporosis therapy for a female by performing (I) and selecting a therapeutic which is a modulator of an IL-1 (preferably of IL-1 alpha, IL-1 beta, IL-1RN) activity (claimed).

The modulator is preferably a protein, peptide, peptidomimetic, small molecule, nucleic acid or a nutraceutical, agonist or an antagonist (claimed).

Information obtained from the assays is useful for determining whether a non-symptomatic subject has or is likely to develop the

09/632657

particular disease or condition, and allows a more customized approach to preventing the onset or progression of the disease or condition and enables the clinician to effectively prescribe a therapy that addresses the molecular basis of the disease or condition. The detection of the alleles can indicate that the subject has or is predisposed to the development of osteoporosis.
Dwg.0/5

L14 ANSWER 3 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:526220 BIOSIS
DOCUMENT NUMBER: PREV200100526220
TITLE: **Polymorphisms** for interleukin-1beta (IL-1beta)-511 promoter, IL-1beta exon 5, and IL-1 receptor antagonist: Nonassociation with endometriosis.
AUTHOR(S): Hsieh, Yao-Yuan; Chang, Chi-Chen; Tsai, Fuu-Jen (1); Wu, Jer-Yuarn; Shi, Yi-Ru; Tsai, Horng-Der; Tsai, Chang-Hai
CORPORATE SOURCE: (1) Department of Pediatrics and Medical Genetics, China Medical College Hospital, No. 2 Yuh-Der Road, Taichung: d0704@hpd.cmch.org.tw Taiwan
SOURCE: Journal of Assisted Reproduction and Genetics, (September, 2001) Vol. 18, No. 9, pp. 506-511. print. ISSN: 1058-0468.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Purpose: We aimed to investigate if interleukin-1beta (IL-1beta) and IL-1 receptor antagonist (IL-1Ra) gene **polymorphism** could be used as markers of susceptibility in endometriosis. Materials and Methods: Women were divided into two groups: 1) endometriosis (n = 120); 2) nonendometriosis groups (n = 103). **Polymorphisms** for IL-1beta-511 promoter, IL-1beta exon 5, and IL-1Ra were detected by polymerase chain reaction. Genotypes and allelic frequencies for these **polymorphisms** in both groups were compared. Results: Proportions of different IL-1 and IL-1Ra **polymorphisms** in both groups were nonsignificantly different. Proportions of C homozygote/heterozygote/T homozygote for IL-1beta-511 promoter in both groups were 1) 21.6/59.1/19.1% and 2) 26.2/50.5/23.3%. Proportions of E1 homozygote/heterozygote/E2 homozygote for IL-1beta exon 5 in both groups were 1) 91.6/5/3.3% and 2) 95.15/4.85/0%. Allele I/II/IV/V for IL-1Ra in both groups were 1) 92.5/5.4/1.6/0.4% and 2) 95.1/3.9/1/0%. Conclusions: Association of endometriosis with IL-1beta-511 promoter, IL-1beta exon 5, and IL-1 receptor antagonist gene **polymorphisms** doesn't exist. These **polymorphisms** are not useful markers for prediction of endometriosis susceptibility.

L14 ANSWER 4 OF 14 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1010689950 JICST-EPlus
TITLE: Etiology, Prevention and Treatment of Postmenopausal osteoporosis.
AUTHOR: KURABAYASHI TAKUMI
CORPORATE SOURCE: Niigatadai I Sankafujinkagakukyoshitsu
SOURCE: Niigata Igakkai Zasshi (Niigata Medical Journal), (2001) vol. 115, no. 4, pp. 122-126. Journal Code: F0877A

Searcher : Shears 308-4994

09/632657

PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Preprint
LANGUAGE: Japanese
STATUS: New

CODEN: NIGZAY; ISSN: 0029-0440

AB The etiology of postmenopausal osteoporosis has not completely been solved. Recent studies showed hypoestrogenic state caused the activation of cytokines (IL-1, IL-6, TNF-.ALPHA., GM-CSF etc.) from monocyte, stromal cells and osteoblast in bone marrow, and activated bone resorption and suppressed bone formation. Hormone replacement therapy (HRT) is the first choice of the treatment for postmenopausal osteoporosis. HRT is effective for not only osteoporosis but also climacteric disturbance and hyperlipidemia. HRT causes the increase of bone mineral density within 2 years, and maintains it after 2 years. Vitamin D receptor gene **polymorphism** (Taq) is useful to detect the effect of HRT for osteoporosis. It is important for us to detect the high risk women for osteoporosis. Ovarian dysfunction, castration and GnRH agonist therapy etc. are risk factors for osteoporosis. Pregnancy and lactation may not be risk factors. There are two factors, i.e. genetic factor and environmental factor, to cause osteoporosis. The evaluation of genetic factor and the improvement of life style are very important to prevent osteoporosis. (author abst.)

L14 ANSWER 5 OF 14 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-271467 [23] WPIDS

DOC. NO. CPI: C2000-082959

TITLE: Determination of susceptibility to, and/or response to therapy for osteoporosis used for increasing bone density comprises determining a combination of estrogen and vitamin D receptors **polymorphism**.

DERWENT CLASS: B04 D16

INVENTOR(S): ROUSSEAU, F

PATENT ASSIGNEE(S): (SIGN-N) SIGNALGENE INC

COUNTRY COUNT: 90

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2000015836	A2	20000323	(200023)*	EN	49
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RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC

MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM

EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ

LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD

SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 9957233	A	20000403	(200034)		
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EP 1114181	A2	20010711	(200140)	EN	
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R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK

NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
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WO 2000015836	A2	WO 1999-CA854	19990915
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Searcher : Shears 308-4994

09/632657

AU 9957233 A
EP 1114181 A2

AU 1999-57233 19990915
EP 1999-944190 19990915
WO 1999-CA854 19990915

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9957233	A Based on	WO 200015836
EP 1114181	A2 Based on	WO 200015836

PRIORITY APPLN. INFO: US 1998-100446P 19980915

AN 2000-271467 [23] WPIDS

AB WO 200015836 A UPAB: 20000516

NOVELTY - Determining susceptibility to, and/or response to therapy for osteoporosis of a human patient comprising determining a combination of estrogen and vitamin D receptors **polymorphism** or a **polymorphism** in linkage disequilibrium in a sample, is new.

DETAILED DESCRIPTION - Determining susceptibility to osteoporosis, and/or response to therapy for osteoporosis of a human patient comprises determining a combination of an estrogen receptor **polymorphism** or a **polymorphism** in linkage disequilibrium and a vitamin D receptor **polymorphism** or a **polymorphism** in linkage disequilibrium in a biological sample from the human patient where the estrogen **polymorphism** is selected from a PvuII **polymorphism** located in intron 1 of the estrogen receptor gene, or a DNA variant, equivalent or **mutation** which shows linkage disequilibrium with one of the allele of the PvuII **polymorphism**, and where the vitamin D receptor **polymorphism** is selected from a BsmI **polymorphism** located in intron 8 of the vitamin D receptor gene or a DNA variant, equivalent or **mutation** which shows linkage disequilibrium with one of the allele of the BsmI **polymorphism**.

INDEPENDENT CLAIMS are also included for the following:

(1) a prognosis kit for determining an outcome of an osteoporosis treatment or prevention program for a human patient comprising:

(a) at least one nucleic acid fragment specific for the estrogen receptor (ESR) where the fragment enables an assessment of the ESR **polymorphism** in intron 1 of the ESR gene; and

(b) at least one nucleic acid fragment specific for vitamin D receptor (VDR) where the fragment enables an assessment of the VDR **polymorphism** in intron 8 of the VDR gene; where a combination of **polymorphisms** at the ESR and VDR genes, or markers in linkage disequilibrium enables determination of the outcome of the treatment; and

(2) an assay for screening and selecting an agent which modulates bone density comprising:

(a) an expression vector comprising a promoter operably linked to a reporter gene, the promoter comprising estrogen receptor and vitamin D receptor response elements affecting the activity of the promoter upon binding of estrogen and vitamin D;

(b) a cell expressing a chosen allele of an estrogen receptor and a chosen allele of a vitamin D receptor, and harboring the vector of (a);

(c) submitting the cell to at least one agent; and

Searcher : Shears 308-4994

09/632657

(d) assaying a level of the reporter gene, where an agent can be selected when the level of the reporter gene is significantly modulated by the presence of the agent.

USE - The method is useful for setting up a screening assay for agents destined to modulate estrogen receptor and/or vitamin D receptor function for the purpose of increasing bone density and/or potentiating an action of an osteoporosis treatment program.
Dwg.0/3

L14 ANSWER 6 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:437912 BIOSIS

DOCUMENT NUMBER: PREV200000437912

TITLE: IL-1 receptor antagonist gene
polymorphism associated with age of
menopause.

AUTHOR(S): van Dijk, S. (1); Stone, K. L.; Hannon, R. A.; Lui, L. L.; Sorrell, J. A.; Eastell, R.; Cummings, S. R.; Duff, G. W.

CORPORATE SOURCE: (1) Interleukin Genetics, Inc., San Antonio, TX USA
SOURCE: Journal of Bone and Mineral Research, (September, 2000) Vol. 15, No. Suppl. 1, pp. S537. print.
Meeting Info.: Twenty-Second Annual Meeting of the American Society for Bone and Mineral Research
Toronto, Ontario, Canada September 22-26, 2000
American Society for Bone and Mineral Research
. ISSN: 0884-0431.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

L14 ANSWER 7 OF 14 MEDLINE

ACCESSION NUMBER: 2000212592 MEDLINE

DOCUMENT NUMBER: 20212592 PubMed ID: 10750554

TITLE: Osteoporotic fractures are associated with an 86-base pair repeat **polymorphism** in the
interleukin-1--receptor antagonist
gene but not with **polymorphisms** in the
interleukin-1beta gene.

AUTHOR: Langdahl B L; Lokke E; Carstens M; Stenkjaer L L;
Eriksen E F

CORPORATE SOURCE: Department of Endocrinology and Metabolism, Aarhus
University Hospital, Aarhus Amtssygehus, Denmark.

SOURCE: JOURNAL OF BONE AND MINERAL RESEARCH, (2000 Mar) 15
(3) 402-14.

Journal code: 8610640. ISSN: 0884-0431.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200006

ENTRY DATE: Entered STN: 20000629

Last Updated on STN: 20000629

Entered Medline: 20000619

AB Interleukin-1beta (IL-1beta) is a potent stimulator of bone resorption, and has been implicated in the pathogenesis of high bone turnover and osteoporosis. IL-1 receptor antagonist (IL-1ra) is a competitive inhibitor of IL-1beta effects and the biological effects of IL-1beta are therefore proportional to

Searcher : Shears 308-4994

09/632657

the ratio IL-1beta/IL-1ra. The coding regions of IL-1beta were examined for sequence variations by SSCP and sequencing after polymerase chain reaction (PCR) of genomic DNA. Three previously described **polymorphisms** (C(-511)-T, G(3877)-A and C(3954)-T) in the IL-1beta gene were determined by restriction fragment length **polymorphism** (RFLP) using Ava I, Aci I, and Taq I after PCR. The 86-base pair repeat **polymorphism** in IL-1ra was examined by PCR and electrophoresis and the T11100-C **polymorphism** in the IL-1ra gene was examined by RFLP using MspAII after PCR. All **polymorphisms** were related to bone mass, biochemical markers of bone turnover, and presence of fracture in a study including 389 osteoporotic patients with vertebral fractures and normal controls. Two normal women were heterozygous for a shift from cytosine to thymine (C3263-T) in exon 4 of the IL-1beta gene. This substitution did not affect the amino acid sequence. We did not find other sequence variations in the IL-1beta gene apart from the already known **polymorphisms**. The distribution of C(-511)-T, G(3877)-A, and C(3954)-T genotypes was similar in the osteoporotic and the normal controls. No significant differences could be shown in bone mass or bone turnover. In the IL-1ra gene almost complete linkage was confirmed between the already known **polymorphisms**: G(1731)-A, G(1821)-A, A(1868)-G, G(1887)-C, T(8006)-C, C(8061)-T, 86 base pair variable number tandem repeat (VNTR), A(9589)-T, and a new **polymorphism**: T(1934)-C. The A1A1/A3 genotypes of the IL-1ra VNTR **polymorphism** were significantly more frequent in osteoporotic patients (56.2%) compared with age-matched normal controls (43.3%) ($\chi^2 = 4.09$; $p = 0.043$). The relative risk of osteoporotic fractures was increased to 1.68 (95% CI, 1.01-2.77) in individuals with A1A1/A3 genotypes. Bone mineral density (BMD) of the lumbar spine was reduced in individuals with A1A1/A3 genotypes ($p = 0.014$, analysis of variance [ANOVA]). The difference in bone mass between A1A1/A3 and A2A1/A2 tended to increase with increasing age. T1100-C genotypes were distributed similarly in osteoporotic patients and normal controls and the **polymorphism** was without effect on bone mass and biochemical markers of bone turnover. In conclusion, an 86-base pair repeat **polymorphism** in the IL-1ra gene is associated with increased risk of osteoporotic fractures. Other **polymorphisms** in the IL-1ra and the IL-1beta genes are not associated with osteoporotic fractures or alterations in bone mass or bone turnover.

L14 ANSWER 8 OF 14 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:886548 SCISEARCH
THE GENUINE ARTICLE: 346YJ
TITLE: IL-1 receptor antagonist gene
polymorphism associated with age of
menopause.
AUTHOR: vanDijk S (Reprint); Stone K L; Hannon R A; Lui L L;
Sorrell J A; Eastell R; Cummings S R; Duff G W
CORPORATE SOURCE: INTERLEUKIN GENET INC, SAN ANTONIO, TX; UNIV CALIF
SAN FRANCISCO, SAN FRANCISCO, CA 94143; UNIV
SHEFFIELD, SHEFFIELD, S YORKSHIRE, ENGLAND
COUNTRY OF AUTHOR: USA; ENGLAND
SOURCE: JOURNAL OF BONE AND MINERAL RESEARCH, (SEP 2000)
Vol. 15, Supp. [1], pp. M341-M341.
Publisher: AMER SOC BONE & MINERAL RES, 2025 M ST, N
W, STE 800, WASHINGTON, DC 20036-3309.

Searcher : Shears 308-4994

09/632657

DOCUMENT TYPE: ISSN: 0884-0431.
FILE SEGMENT: Conference; Journal
LANGUAGE: LIFE
REFERENCE COUNT: English
0

L14 ANSWER 9 OF 14 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001107468 MEDLINE
DOCUMENT NUMBER: 21040326 PubMed ID: 11196702
TITLE: Linkage of human tumor necrosis factor-alpha to human
osteoporosis by sib pair analysis.
AUTHOR: Ota N; Hunt S C; Nakajima T; Suzuki T; Hosoi T; Orimo
H; Shirai Y; Emi M
CORPORATE SOURCE: Department of Molecular Biology, Institute of
Gerontology, Nippon Medical School, 1-396 Kosugi-cho,
Nakahara-ku, Kawasaki 211-8533, Japan.
CONTRACT NUMBER: 1-P41-RR03655 (NCRR)
SOURCE: GENES AND IMMUNITY, (2000) 1 (4) 260-4.
Journal code: 100953417. ISSN: 1466-4879.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

AB Osteoporosis as well as osteopenia are common human conditions considered to result from the interplay of multiple genetic and environmental factors. Twin and family studies have yielded strong correlation between measures of bone mass and a number of genetic factors. Certain genes (e.g., cytokines such as **interleukin -1**, interleukin-6, or tumor necrosis factor-alpha) are capable of regulating metabolism, formation, and resorption of bone; all processes that determine bone mass. We tested 192 sib-pairs of adult Japanese women from 136 families for genetic linkage between osteoporosis and osteopenia phenotypes and **allelic variants** at the tumor necrosis factor-alpha (TNFA) locus, using a dinucleotide-repeat **polymorphism** located near the gene. The TNFA locus showed evidence for linkage to osteoporosis, with mean allele sharing of 0.478 ($P = 0.30$) in discordant pairs and 0.637 ($P = 0.001$) in concordant affected pairs. Linkage with osteopenia was also significant in concordant affected pairs ($P = 0.017$). Analyses limited to the post-menopausal women in our cohort showed similar or even stronger linkage for both phenotypes. The results provide evidence that genetic variations within the TNFA locus or adjacent genes affect regulation of mineral metabolism in bone and some of them confer risk for osteoporosis in adult women.

L14 ANSWER 10 OF 14 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998434113 MEDLINE
DOCUMENT NUMBER: 98434113 PubMed ID: 9763149
TITLE: **Allelic variation** at the
interleukin-1 receptor antagonist
gene is associated with early postmenopausal bone
loss at the spine.
AUTHOR: Keen R W; Woodford-Richens K L; Lanchbury J S;

Searcher : Shears 308-4994

09/632657

CORPORATE SOURCE: Spector T D
Twin & Genetic Epidemiology Research Unit, St.
Thomas' Hospital, London, UK.. r.keen@umds.ac.uk
SOURCE: BONE, (1998 Oct) 23 (4) 367-71.
Journal code: 8504048. ISSN: 8756-3282.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981204

AB Genetic factors play an important role in determining bone mineral density (BMD) in later life, with the genetic influence mediated through effects on both peak mass and on age- and **menopause**-related bone loss. At **menopause** there is an increase in the production and activity of various cytokines and growth factors within the bone microenvironment. The activity of **interleukin-1 (IL-1)**, a powerful stimulant of osteoclastic bone resorption, is increased in estrogen-deficient states with increased production of **IL-1** and inhibition of the **IL-1** receptor antagonist (IL-1ra). Treatment with IL-1ra blocks the bone loss associated with ovariectomy in animals and the **IL-1** receptor antagonist gene (**IL-1RN**) is therefore a potential candidate gene for the regulation of postmenopausal bone loss. We examined the relationship between annual rates of change in BMD over 5 years and an 86 bp variable number tandem-repeat **polymorphism** of the **IL-1RN** gene in 108 early postmenopausal women. All women were within 5 years of a natural **menopause** at the study's onset, healthy, and not on hormone replacement therapy or other medication known to affect bone metabolism. BMD was measured annually over the 5 year study period at the lumbar spine and femoral neck using dual-energy X-ray absorptiometry. Three alleles were identified (A1 = 4 repeats, A2 = 2 repeats, A3 = 5 repeats), with five genotypes observed: A1A1 (41.7%), A1A2 (45.4%), A2A2 (6.5%), A1A3 (2.8%), and A2A3 (3.7%). For analysis, alleles were collapsed into a biallelic system grouping the A1 and A3 alleles. There was no significant relationship between the **IL-1RN** genotypes and baseline bone mass at either the spine or hip. **IL-1RN** genotype was significantly associated with annual rates of change in spinal bone mass ($p < 0.05$), and this finding remained significant after adjustment for age, weight, and baseline BMD. Carriage of at least one copy of the A2 allele was associated with reduced bone loss at the spine (mean change in BMD \pm SD: $-0.81 \pm 1.46\%$ /year) when compared with noncarriage of the A2 allele (mean change $-1.38 \pm 1.48\%$ /year), $p = 0.05$. We therefore conclude that **allelic variation** at the **IL-1RN** locus is associated with differential rates of early postmenopausal bone loss at the spine. Further research will be required to clarify the mechanisms underlying these findings and to determine whether this association translates into a significant long-term effect on BMD and fracture in later life.

L14 ANSWER 11 OF 14 SCISEARCH COPYRIGHT 2002 ISI (R)

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09/632657

ACCESSION NUMBER: 97:685506 SCISEARCH
THE GENUINE ARTICLE: XP627
TITLE: Early **menopausal** bone loss at the spine is associated with **polymorphism** at the **interleukin 1** receptor antagonist locus
AUTHOR: Keen R W (Reprint); WoodfordRichens K L; Major P J; Lanchbury J S; Spector T D
CORPORATE SOURCE: ST THOMAS HOSP, TWIN & OSTEOPOROSIS RES UNIT, LONDON, ENGLAND; UMDS, MOL IMMUNOGENET UNIT, LONDON, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: JOURNAL OF BONE AND MINERAL RESEARCH, (AUG 1997) Vol. 12, Supp. [1], pp. T620-T620. Publisher: BLACKWELL SCIENCE INC, 350 MAIN ST, MALDEN, MA 02148. ISSN: 0884-0431.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 0

L14 ANSWER 12 OF 14 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97263849 EMBASE
DOCUMENT NUMBER: 1997263849
TITLE: Changes of bone metabolism with ageing in relation to involvement of estrogen withdrawal.
AUTHOR: Gorai I.
CORPORATE SOURCE: I. Gorai, Department of Obstetrics/Gynecology, Yokohama City Univ. School of Med., Yokohama, Japan
SOURCE: Acta Obstetrica et Gynaecologica Japonica, (1997) 49/8 (537-545). ISSN: 0300-9165 CODEN: AOGLAR
COUNTRY: Japan
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
020 Gerontology and Geriatrics
033 Orthopedic Surgery
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese

AB The diminution of bone mineral density (BMD) in women is initiated at the onset of **menopause** and estrogen withdrawal causes rapid bone loss in early postmenopausal years, leading to an increase in a risk of osteoporotic fracture. Several cytokines are considered to be involved in the decrease of BMD due to estrogen deficiency. Recently, it has been reported that estrogen is important for bone maturation and mineralization in men as well as in women. In this study, we investigated the involvement of estrogen deficiency in bone metabolism of postmenopausal women as compared with **premenopausal** women and assessed the factors relating to postmenopausal bone loss. In experimental study, at 4 weeks after ovariectomy (OVX), in OVX mice, femoral BMD decreased whereas the number of bone marrow cells was greatly increased. To explore the endogenous bone-resorbing factors involved in estrogen deficiency, we examined the bone-resorbing activity in the supernatant fraction of mouse bone marrow collected from ovariectomized mice. Only anti-interleukin (IL)-1.alpha. antibody completely

Searcher : Shears 308-4994

neutralized the bone-resorbing activity in bone marrow supernatants from OVX mice. The concurrent addition of **IL-1**, **IL-6**, s**IL-6** receptor (R) and prostaglandin (PG)E2 co-operatively induced bone resorption. The effect of L-2.alpha. on collagenase and gelatinase activities and matrix metalloproteinase (MMP)-2 and MMP-13 mRNA expression was analyzed using **IL-1** .alpha. supplemented medium of organ culture of newborn mouse calvaria and osteoblasts from newborn mouse calvaria, respectively. **IL-1** .alpha. increased collagenase and gelatinase activities as compared with those of control medium and stimulated MMP-2 and MMP-13 mRNA expression. Human osteoblast-like cells, HOS TE 85 cells, showed aromatase activity, which was determined using 3H-androstenedione as a substrate and addition of retinoic acid, TPA, bone morphogenic protein (BMP)-2 and dexamethasone increased their aromatase activity. As determined by RT-PCR method, retinoic acid and TPA increased aromatase mRNA expression of HOS TE 85 cells. At 3 weeks after orchidectomy (ORX), in ORX mice, the weight of seminal vesicles and femoral BMD decreased whereas the number of bone marrow cells was greatly increased. The change of hemopoiesis and bone metabolism induced by ORX were completely restored by the treatment with 1 .mu.g of E2 but not with 10 .mu.g of DHT. In clinical study, several risk factors relating to low bone mass were assessed. Lumbar spine BMD significantly correlated with years since **menopause** (YSM) ($r = -0.366$), body weight ($r = 0.350$), age ($r = -0.340$), body mass index (BMI) ($r = 0.242$), and height ($r = 0.212$) in the postmenopausal women. In order to investigate an association between vitamin D receptor (VDR) gene **polymorphism** and BMD or bone loss, we examined VDR Bsm1 RFLP with amplification refractory **mutation** system (ARMS) and could not find any significant differences in lumbar spine baseline BMD between the bb genotype and the Bb genotype. In both early and late postmenopausal periods vertebral BMD with the Bb genotype decreased faster than that with the bb genotype ($p = 0.001$). When we divided the subjects whose ages were from 45 to 55 years into two subgroups (pre- and postmenopausal) to assess the effects of **menopause** on biochemical markers of bone resorption, we found a significant 110% increase in crosslinked N- telopeptides of type I collagen (NTx) and a 48% increase in lysylpyridinoline (LP) in post-**menopausal** women compared with age-matched **premenopausal** women. The ROC analysis showed that the cutoff BMD values for discrimination of women with vertebral fracture varied according to the sites and methods of measurement ranging 59.0% of young adult mean value (YAM) of radial trabecular BMD by pQCT to 83.8% of young adult mean value (YAM) of femoral neck BMD by DXA.

L14 ANSWER 13 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1997:239623 BIOSIS
 DOCUMENT NUMBER: PREV199799538826
 TITLE: Early **menopausal** bone loss at the spine is associated with **polymorphisms** at the **interleukin 1** receptor antagonist locus but not the interleukin 6 locus.
 AUTHOR(S): Woodford-Richens, K. L. (1); Keen, R. W. (1); Lanchbury, J. S. (1); Spector, T. D.
 CORPORATE SOURCE: (1) Mol. Immunogenet. Unit, UMDS, Guy's Hosp., London SE1 9RT UK
 SOURCE: Bone (New York), (1997) Vol. 20, No. 4 SUPPL., pp.

09/632657

8S.

Meeting Info.: 25th European Symposium on Calcified
Tissues Harrogate, England, UK April 25-29, 1997
ISSN: 8756-3282.

DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L14 ANSWER 14 OF 14 MEDLINE

ACCESSION NUMBER: 97133753 MEDLINE

DOCUMENT NUMBER: 97133753 PubMed ID: 8979148

TITLE: Estriol: a potent regulator of TNF and IL-6
expression in a murine model of endotoxemia.

AUTHOR: Zuckerman S H; Ahmari S E; Bryan-Poole N; Evans G F;
Short L; Glasebrook A L

CORPORATE SOURCE: Division of Cardiovascular Research, Lilly Research
Labs, Indianapolis, Indiana 46285, USA.

SOURCE: INFLAMMATION, (1996 Dec) 20 (6) 581-97.
Journal code: 7600105. ISSN: 0360-3997.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199704

ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970402

AB The increased incidence of autoimmune disease in
premenopausal women suggests the involvement of sex steroids
in the pathogenesis of these disease processes. The effects of
estrogen on autoimmunity and inflammation may involve changes in the
secretion of inflammatory mediators by mononuclear phagocytes.
Estradiol, for example, has been reported to regulate TNF, IL-6,
IL-1 and JE expression. In the present study the
effects of the estrogen agonist, estriol, on cytokine expression
have been investigated in mice administered a sublethal
lipopolysaccharide, LPS, challenge. Pretreatment of mice with
pharmacologic doses of estriol, 0.4-2 mg/kg, resulted in a
significant increase in serum TNF levels in both control and
autoimmune MRL/lpr mice, following LPS challenge. This increase in
TNF over the placebo group was blocked by the estrogen antagonist
tamoxifen. Estriol treated mice also exhibited a rapid elevation in
serum IL-6 levels following LPS challenge with the peak increase
occurring 1 hr post LPS. This contrasted with the placebo group in
which maximal serum IL-6 levels were detected at 3 hrs post
challenge. This shift in the kinetics of IL-6 increase by estriol
was inhibited by tamoxifen. The estriol mediated effects of TNF and
IL-6 serum levels were consistent with the changes in TNF and IL-6
mRNA observed ex vivo in elicited peritoneal macrophages. Macrophage
cultures from estriol treated animals however, did not demonstrate
significant differences from the placebo group for TNF or NO
secretion following in vitro LPS challenge. These results suggest
that the estrogen agonist estriol can have significant quantitative,
TNF, and kinetic, IL-6, effects on inflammatory monokines produced
in response to an endotoxin challenge.

(FILE 'MEDLINE' ENTERED AT 15:34:33 ON 18 JUL 2002)

L15 24511 SEA FILE=MEDLINE ABB=ON PLU=ON INTERLEUKIN-1/CT
L16 15086 SEA FILE=MEDLINE ABB=ON PLU=ON MENOPAUSE/CT

Searcher : Shears 308-4994

09/632657

L17 2321 SEA FILE=MEDLINE ABB=ON PLU=ON PREMENOPAUSE/CT
L18 16 SEA FILE=MEDLINE ABB=ON PLU=ON L15 AND (L16 OR L17)

L18 ANSWER 1 OF 16 MEDLINE

AN 2001173753 MEDLINE

TI Interleukin-1beta-induced prostaglandin E2 production in human myometrial cells: role of a pertussis toxin-sensitive component.

AU Hertelendy F; Rastogi P; Molnar M; Romero R

SO AMERICAN JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (2001 Mar) 45 (3) 142-7.

Journal code: 8912860. ISSN: 1046-7408.

AB PROBLEM: The objective of this study was to evaluate the possible role of pertussis toxin (PTX)-sensitive G-protein(s) in interleukin-1beta (IL-1) signaling in human myometrial cells (HMC). METHOD: Primary cultures of HMC were stimulated with human recombinant IL-1 alone or in combination with PTX. Prostaglandin (PG) E2 in the medium was measured by radioimmunoassay, cyclooxygenase type 2 (Cox-2) and IkappaB by western analysis, and the activities of two members of the mitogen-activated protein kinase (MAPK) family of enzymes, ERK-2 and JNK, by the phosphorylation of appropriate substrates. RESULTS: IL-1 increased PGE2 output during an 18-hr long incubation by 21.7-fold (n = 5 experiments). This increase was inhibited by 57% after pretreatment overnight with PTX. IL-1-induced expression of Cox-2 protein was also suppressed to a similar degree in PTX-treated HMC cultures. Degradation of the nuclear factor kappa B (NF-kappaB)-inhibiting protein (IkappaB), a critical step in IL-1 signaling to the nucleus, was significantly inhibited by PTX, as was IL-1-induced activation of ERK-2 and JNK. CONCLUSIONS: It is suggested that the occupied IL-1 receptor-generated signal in HMC is transmitted by multiple pathways. One is coupled to a PTX-sensitive G-protein upstream from the MAPK phosphorylation cascade. This, in turn, may interact with another signaling pathway, the activation of NF-kappaB, via the phosphorylation of the IkappaB kinase complex.

L18 ANSWER 2 OF 16 MEDLINE

AN 2000212592 MEDLINE

TI Osteoporotic fractures are associated with an 86-base pair repeat polymorphism in the interleukin-1--receptor antagonist gene but not with polymorphisms in the interleukin-1beta gene.

AU Langdahl B L; Lokke E; Carstens M; Stenkjaer L L; Eriksen E F

SO JOURNAL OF BONE AND MINERAL RESEARCH, (2000 Mar) 15 (3) 402-14.

Journal code: 8610640. ISSN: 0884-0431.

AB Interleukin-1beta (IL-1beta) is a potent stimulator of bone resorption, and has been implicated in the pathogenesis of high bone turnover and osteoporosis. IL-1 receptor antagonist (IL-1ra) is a competitive inhibitor of IL-1beta effects and the biological effects of IL-1beta are therefore proportional to the ratio IL-1beta/IL-1ra. The coding regions of IL-1beta were examined for sequence variations by SSCP and sequencing after polymerase chain reaction (PCR) of genomic DNA. Three previously described polymorphisms (C(-511)-T, G(3877)-A and C(3954)-T) in the IL-1beta gene were determined by restriction fragment length polymorphism (RFLP) using Ava I, Acl I, and Taq I after PCR. The 86-base pair repeat polymorphism in IL-1ra was examined by PCR and electrophoresis and the T11100-C polymorphism in the IL-1ra gene was examined by RFLP using MspAII after PCR. All polymorphisms were related to bone mass, biochemical markers of bone turnover, and presence of fracture in a study

including 389 osteoporotic patients with vertebral fractures and normal controls. Two normal women were heterozygous for a shift from cytosine to thymine (C3263-T) in exon 4 of the IL-1beta gene. This substitution did not affect the amino acid sequence. We did not find other sequence variations in the IL-1beta gene apart from the already known polymorphisms. The distribution of C(-511)-T, G(3877)-A, and C(3954)-T genotypes was similar in the osteoporotic and the normal controls. No significant differences could be shown in bone mass or bone turnover. In the IL-1ra gene almost complete linkage was confirmed between the already known polymorphisms: G(1731)-A, G(1821)-A, A(1868)-G, G(1887)-C, T(8006)-C, C(8061)-T, 86 base pair variable number tandem repeat (VNTR), A(9589)-T, and a new polymorphism: T(1934)-C. The A1A1/A3 genotypes of the IL-1ra VNTR polymorphism were significantly more frequent in osteoporotic patients (56.2%) compared with age-matched normal controls (43.3%) ($\chi^2 = 4.09$; $p = 0.043$). The relative risk of osteoporotic fractures was increased to 1.68 (95% CI, 1.01-2.77) in individuals with A1A1/A3 genotypes. Bone mineral density (BMD) of the lumbar spine was reduced in individuals with A1A1/A3 genotypes ($p = 0.014$, analysis of variance [ANOVA]). The difference in bone mass between A1A1/A3 and A2A1/A2 tended to increase with increasing age. T1100-C genotypes were distributed similarly in osteoporotic patients and normal controls and the polymorphism was without effect on bone mass and biochemical markers of bone turnover. In conclusion, an 86-base pair repeat polymorphism in the IL-1ra gene is associated with increased risk of osteoporotic fractures. Other polymorphisms in the IL-1ra and the IL-1beta genes are not associated with osteoporotic fractures or alterations in bone mass or bone turnover.

- L18 ANSWER 3 OF 16 MEDLINE
 AN 2000141876 MEDLINE
 TI Cytokine RNA levels in transiliac bone biopsies from healthy early postmenopausal women.
 AU Abrahamsen B; Shalhoub V; Larson E K; Eriksen E F; Beck-Nielsen H; Marks S C Jr
 SO BONE, (2000 Feb) 26 (2) 137-45.
 Journal code: 8504048. ISSN: 8756-3282.
 AB The cytokines interleukin-1beta (IL-1beta), tumor necrosis factor-alpha (TNF-alpha), and IL-6 induce osteoclast formation and may contribute to the development of postmenopausal osteoporosis. Cross-sectional studies have suggested that both IL-1 and IL-1ra secretion increase on estrogen withdrawal, and that postmenopausal osteoporosis is associated with an inadequate increase in monocyte IL-1ra secretion with age. We measured cytokine mRNA (IL-1beta, IL-1ra, IL-6, and TNF-alpha) directly in bone biopsies from early postmenopausal women to determine if a lower compensatory increase in IL-1ra mRNA could be demonstrated in women with rapid bone loss after the menopause. Biopsies were obtained from 23 early postmenopausal women (mean age 53.9 years) who participated in a randomized study of hormone replacement therapy (HRT) and risk factors for osteoporosis. Bone mineral density was assessed by dual energy X-ray absorptiometry at 0, 1, 2, and 5 years. Women in the control group were recruited to the biopsy study based on their observed rate of bone loss (upper or lower tertile). Consent was also obtained from 11 participants receiving HRT. Biopsies were taken at 2 years, frozen in nitrogen, and homogenized. Cytokine mRNA was measured by competitive reverse transcriptase polymerase chain reaction. The IL-1ra/IL-1beta mRNA slope for the slow-loss group was

09/632657

steeper ($\Delta F = 23.3$, $p < 0.01$) than that observed in the fast-loss group, indicating that slower bone loss was associated with higher IL-1ra mRNA levels relative to IL-1beta. During HRT, the IL-1beta mRNA level was inversely correlated with serum estradiol ($\log r_2 = 0.77$, $p < 0.01$), and women with a serum estradiol below 200 pmol/L during HRT had IL-1beta, mRNA levels identical to the control group. In contrast, IL-1ra mRNA was independent of serum estradiol. Histomorphometric analysis revealed weak correlations between IL-1beta mRNA and activation frequency ($r_2 = 0.26$, $p = 0.06$) and between IL-1ra and volume referent bone resorption rate ($r_2 = 0.19$, $p = 0.11$). TNF-alpha was not associated with the bone loss rates or with serum estradiol, and only three samples were positive for IL-6 mRNA. The findings support the hypothesis that IL-1beta production within bone increases with declining estrogen levels, and that an increase in IL-1ra protects against accelerated bone loss.

L18 ANSWER 4 OF 16 MEDLINE
AN 2000009315 MEDLINE
TI Aging and cytokine production.
AU Pacifici R
SO CALCIFIED TISSUE INTERNATIONAL, (1999 Nov) 65 (5) 345-51.
Journal code: 7905481. ISSN: 0171-967X.

L18 ANSWER 5 OF 16 MEDLINE
AN 1999306464 MEDLINE
TI Bladder infection in the menopausal monkey.
AU Roberts J A; Kaack M B; Harrison R M; Klopp R; Ershler W
SO JOURNAL OF UROLOGY, (1999 Jul) 162 (1) 254-7.
Journal code: 0376374. ISSN: 0022-5347.
AB PURPOSE: The highest incidence of urinary tract infection in females occurs in elderly women. This study was done to determine whether this is due to the declining immune response that occurs during advancing age, or the menopausal state in the aged. MATERIALS AND METHODS: Adult female monkeys (average age 19 years) were studied, half being subjected to bilateral oophorectomy to produce the menopause. In addition, old females (average age 29 years) already at menopause were studied before and after hormonal replacement with estradiol and progesterone. Bacterial adherence to vaginal cells was studied prior to and after urethral infection with E. coli. Plasma estradiol and progesterone levels were done, as well as white blood counts, plasma cytokine assays and serum antibody titers. RESULTS: Bacteriuria was not prolonged, nor was there a significant difference in bacterial adherence to vaginal cells due to menopause. Interleukin-1 levels were depressed after surgical menopause but not as much as found in the old menopausal females and this low level was not corrected by hormonal replacement. The initial interleukin-2 levels were higher after spontaneous menopause, but the increasing plasma levels seen in cycling animals after infection did not occur in the aged menopausal females following infection even after hormone replacement. The antibody titers to the E. coli infection showed a trend to a lessened response to infection after menopause but were not significantly decreased. CONCLUSIONS: The deficient IL-1, IL-2 and antibody response following infection was not corrected by hormone replacement and thus appears to be due to aging rather than lack of female hormones. These facts may be explained by the T cell senescence known to occur in aged individuals.

L18 ANSWER 6 OF 16 MEDLINE

Searcher : Shears 308-4994

09/632657

AN 1999036692 MEDLINE
TI Cytokine production and bone mineral density at the lumbar spine and femoral neck in premenopausal women.
AU Salamone L M; Whiteside T; Friberg D; Epstein R S; Kuller L H; Cauley J A
SO CALCIFIED TISSUE INTERNATIONAL, (1998 Dec) 63 (6) 466-70.
Journal code: 7905481. ISSN: 0171-967X.
AB Cytokines such as interleukin-1 (IL-1beta), interleukin-6 (IL-6) and tumor necrosis factor (TNF-alpha) can influence both bone resorption and bone formation. The objective of this cross-sectional study was to examine the relationship between cytokine production by peripheral blood mononuclear cells (PBMC) and bone mineral density (BMD); the annual rate of change in BMD was examined. Subjects participating in a randomized clinical trial entitled the Women's Healthy Lifestyle Project in Allegheny County, Pennsylvania were used. They included 50 healthy premenopausal women, aged 45-52 years, who had regular menses within the past 3 months and were not on replacement estrogens. Dual-energy X-ray absorptiometry measurements at the AP lumbar spine and femoral neck were made at baseline and at the first annual exam using a Hologic QDR 2000 densitometer. Cytokine production of IL-1beta, IL-6, and TNF-alpha by PBMC was measured at the annual exam. The median values for stimulated cytokine production by PBMC were 3.92 ng/ml, 31.3 ng/ml, and 1.05 ng/ml, for IL-1beta, IL-6, and TNF-alpha, respectively. There were modest correlations between cytokine production and cross-sectional BMD, ranging from $r = -0.30$ to $r = -0.13$. Trends of greater spinal bone loss were observed in women with "high" (≥ 75 th percentile) cytokine production of stimulated IL-1beta and IL-6 (IL-1beta: "high" = $-1.56\% \pm 0.70$ versus "low" (< 75 th percentile) = $-0.56\% \pm 0.35$, $P = 0.21$). In contrast, greater annual gains in femoral neck BMD were observed in those with high cytokine production of IL-1beta and IL-6 (IL-1beta: high = $3.39\% \pm 1.16$ versus low = -0.85 ± 0.58 , $P = 0.002$). There was no association between stimulated TNF production and annual change in BMD. In this population of healthy premenopausal women, the relationship between cytokine production by PBMC and the rate of change in BMD was significantly different for the lumbar spine and femoral neck, possibly reflecting differences in the proportion of trabecular and cortical bone at these sites.

L18 ANSWER 7 OF 16 MEDLINE
AN 95203486 MEDLINE
TI Stimulation of aromatase activity in breast fibroblasts by tumor necrosis factor alpha.
AU Macdiarmid F; Wang D; Duncan L J; Purohit A; Ghilchick M W; Reed M J
SO MOLECULAR AND CELLULAR ENDOCRINOLOGY, (1994 Dec) 106 (1-2) 17-21.
Journal code: 7500844. ISSN: 0303-7207.
AB The conversion of androstenedione to estrone, the reaction mediated by the aromatase enzyme complex, may make an important contribution to the synthesis of estrogens in breast tissues. In the present study, the effect of the cytokine. TNF alpha, on aromatase activity was examined in breast fibroblasts derived from normal and malignant breast tissue. TNF alpha (2.5-10.0 ng/ml), in the presence of stripped fetal calf serum and dexamethasone, significantly stimulated fibroblast aromatase activity in a dose-dependent manner. IL-1 and IL-6 also stimulated fibroblast aromatase activity, but no marked synergism between TNF alpha and IL-1 or IL-6 was detected. Using a specific radioimmunoassay, significant concentrations of TNF

09/632657

alpha were detected in samples of breast cyst fluid and breast tumor cytosol, which had previously been shown to stimulate aromatase activity, but not in conditioned medium from breast tumor-derived fibroblasts. As TNF alpha may be preferentially expressed and produced in the adipose tissue component of the breast, this cytokine may have an important role in regulating estrogen synthesis in normal and malignant breast tissues.

- L18 ANSWER 8 OF 16 MEDLINE
AN 95067031 MEDLINE
TI Circulating levels of cytokines that modulate bone resorption: effects of age and menopause in women.
AU McKane W R; Khosla S; Peterson J M; Egan K; Riggs B L
SO JOURNAL OF BONE AND MINERAL RESEARCH, (1994 Aug) 9 (8) 1313-8.
Journal code: 8610640. ISSN: 0884-0431.
AB Interleukin 1 alpha (IL-1 alpha), interleukin 1 beta (IL-1 beta), and interleukin 6 (IL-6) are cytokines with potent bone-resorbing effects; some of these biologic effects are opposed by interleukin-1 receptor antagonist (IL-1ra). In vitro and animal model studies suggest that these cytokines are paracrine mediators of the increased bone resorption associated with estrogen deficiency, and increases in their production also could contribute to age-related bone loss. Therefore, we measured serum concentrations of these cytokines in 80 normal women who were 24-87 years old. IL-6 concentration correlated highly with age ($p < 0.001$) and increased three-fold during life. However, multiple-regression analysis showed no significant correlation between serum IL-6 levels and menopausal status, serum estradiol concentration, or markers for bone turnover (serum bone alkaline phosphatase, osteocalcin, carboxyl-terminal telopeptide of type I collagen, or 24 h urinary free pyridinoline excretion). Serum IL-1 alpha, IL-1 beta, or IL-1ra level did not change with age and, by multiple-regression analysis, did not correlate with markers of bone turnover, except IL-1ra weakly with ICTP. We found no relationship between bone-resorbing cytokines and ovarian function. Although the large age-related increase in serum IL-6 concentration could contribute to age-related bone loss, the lack of correlation with markers for bone turnover argues against this. However, based on the strong evidence in experimental animals that these cytokines are involved in estrogen action on bone, further studies in humans are warranted.
- L18 ANSWER 9 OF 16 MEDLINE
AN 94358009 MEDLINE
TI Monocytic secretion of interleukin-1 receptor antagonist in normal and osteoporotic women: effects of menopause and estrogen/progesterone therapy.
AU Pacifici R; Vannice J L; Rifas L; Kimble R B
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1993 Nov) 77 (5) 1135-41.
Journal code: 0375362. ISSN: 0021-972X.
AB Interleukin-1 (IL-1), a potent stimulant of bone resorption, has been implicated in the pathogenesis of postmenopausal osteoporosis, because monocyte IL-1 bioactivity increases after the menopause and is decreased by estrogen and progesterone (EP) replacement. As IL-1 bioactivity reflect the production of both IL-1 and the IL-1 inhibitor, IL-1 receptor antagonist (IL-1ra), EP treatment could decrease IL-1 bioactivity by regulating the secretion of either IL-1 or IL-1ra. We now report that EP treatment in vivo decreased the

09/632657

secretion into the medium of cultured monocytes of IL-1ra and IL-1 beta as well as the IL-1 beta/IL-1ra ratio. We also found that in normal women the production of IL-1ra was within premenopausal levels in the first 7 yr after the menopause and increased linearly thereafter. In these women, monocyte IL-1 beta, IL-1 beta/IL-1ra ratio, and IL-1 bioactivity were all increased in the first 7 yr after the menopause and within the premenopausal range thereafter. In osteoporotic women, IL-1 beta, IL-1 beta/IL-1ra ratio, and IL-1 bioactivity increased after the menopause and returned to premenopausal levels after 15 yr from the menopause. In these women monocyte IL-1ra secretion was above the premenopausal range at all times after the menopause, but did not change with the passage of time since menopause. We conclude that hormone replacement decreases the in vitro secretion of both IL-1ra and IL-1 beta. The data also suggest that in normal women a progressive increase in the secretion of IL-1ra contributes to restore a normal IL-1/IL-1ra ratio after the menopause, a phenomenon which, in turn, may play a role in limiting postmenopausal bone loss.

L18 ANSWER 10 OF 16 MEDLINE

AN 94172090 MEDLINE

TI Gingival fluid IL-1 beta and IL-6 levels in menopause.

AU Reinhardt R A; Masada M P; Payne J B; Allison A C; DuBois L M

SO JOURNAL OF CLINICAL PERIODONTOLOGY, (1994 Jan) 21 (1) 22-5.

Journal code: 0425123. ISSN: 0303-6979.

AB Menopause and oophorectomy without estrogen therapy (ED) have been associated with increased production of bone-active cytokines by peripheral blood mononuclear cells. The current study extended evaluation to gingival crevicular fluid (GCF) levels of interleukin (IL)-1 beta and IL-6 in such subjects compared to premenopausal and postmenopausal estrogen-treated females (ES). 13 ED and 13 ES Caucasians with a history of moderate-severe adult periodontitis provided GCF from 1-3 clinically identical sites each (5-6 mm probing depth, 5-7 mm clinical attachment loss, bleeding on probing). 30 s GCF samples were obtained and evaluated for IL-1 beta and IL-6 levels using two-site enzyme-linked immunosorbent assays (ELISAs). The frequency of GCF IL-1 beta-positive subjects was elevated in ED versus ES (92% versus 23%; $p < 0.0004$, chi 2 analysis). IL-6 was detected more frequently in ED subjects (23% versus 8%; not significant); however, the frequency of IL-6 detection was low in both groups due to short sampling times. These data support the concept that clinical conditions causing low estrogen environments allow increased local production of the bone-active cytokine IL-1 beta, and perhaps IL-6.

L18 ANSWER 11 OF 16 MEDLINE

AN 94086760 MEDLINE

TI Peripheral monocyte culture supernatants of menopausal women can induce bone resorption: involvement of cytokines.

AU Cohen-Solal M E; Graulet A M; Denne M A; Gueris J; Baylink D; de Vernejoul M C

SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1993 Dec) 77 (6) 1648-53.

Journal code: 0375362. ISSN: 0021-972X.

AB Increased bone resorption is a mechanism contributing to bone loss in the postmenopausal period. Cytokines are involved in osteoclastic differentiation and, therefore, may play a role in the regulation of bone resorption. Several previous works showed the implication of

interleukin-1 (IL-1), IL-6, and tumor necrosis factor-alpha (TNF alpha) in the modulation of bone remodeling. This study determines the concomitant production of the three cytokines and tests the bone-resorbing activity of peripheral monocyte supernatants. Four groups of women were studied: premenopausal women (n = 13; mean age, 47 +/- 0.9 yr), untreated postmenopausal women (n = 21; mean age, 52 +/- 0.6 yr), postmenopausal women treated with estrogens (n = 14; mean age, 54.2 +/- 1.1 yr), or postmenopausal women treated with ethanehydroxydiphosphonate (n = 12; mean age, 53.2 +/- 2 yr). Assignment to clinical groups was verified by plasma FSH and estradiol determinations. Lumbar spine bone mineral density was significantly higher in the premenopausal women group than in the three postmenopausal groups. Peripheral blood monocytes were cultured for 48 h with 20% autologous plasma, and after stimulation with lipopolysaccharides. IL-1, IL-6, and TNF alpha levels were measured by RIA in the monocyte supernatants. The three cytokines were highly correlated to each other, IL-1 with IL-6 (r = 0.76; P < 0.001), IL-1 with TNF alpha (r = 0.89; P < 0.001), and IL-6 with TNF alpha (r = 0.89; P < 0.001). The mean levels of the three cytokines could not be compared because of the variations in the values. However, a trend toward lower levels in the three cytokines was noted in estrogen-treated women compared to the untreated postmenopausal women. The bone-resorbing activity of monocyte supernatants, assessed by fetal long bone-resorbing assay, increased in untreated postmenopausal compared to that in premenopausal women (1.22 +/- 0.08 vs. 0.87 +/- 0.11; P < 0.05). In estrogen-treated patients, this activity decreased to premenopausal levels (0.89 +/- 0.04 vs. 0.87 +/- 0.11; P = NS). The resorbing activity was correlated to IL-1 (r = 0.28; P = 0.03), IL-6 (r = 0.52; P < 0.01), and TNF alpha (r = 0.48; P < 0.01). The addition of cytokine inhibitors and IL-1 receptor antagonist and TNF alpha antibodies to the supernatant bone culture medium induced a significant decrease in the calcium release. Those data show the involvement of several cytokines in the bone resorption process after estrogen deficiency.

- L18 ANSWER 12 OF 16 MEDLINE
 AN 94076121 MEDLINE
 TI Gingival crevicular fluid IL-8: correlation with local IL-1 beta levels and patient estrogen status.
 AU Payne J B; Reinhardt R A; Masada M P; DuBois L M; Allison A C
 SO JOURNAL OF PERIODONTAL RESEARCH, (1993 Nov) 28 (6 Pt 1) 451-3.
 Journal code: 0055107. ISSN: 0022-3484.
 AB Gingival crevicular fluid (GCF) IL-8 and IL-1 beta levels were determined by sandwich enzyme-linked immunosorbent assays. Associations between IL-8 and IL-1 beta GCF levels, and between these cytokines and patient estrogen status were evaluated. IL-8 and IL-1 beta were detected more frequently and in higher amounts/30 s GCF sample in estrogen-deficient patients than in estrogen-sufficient patients. IL-8 and IL-1 beta GCF levels were significantly correlated. These findings suggest that GCF IL-8 levels are associated with patient estrogen status and local IL-1 beta concentrations.
- L18 ANSWER 13 OF 16 MEDLINE
 AN 94056531 MEDLINE
 TI Interleukin-1 and tumor necrosis factor stimulate arachidonic acid release and phospholipid metabolism in human myometrial cells.
 AU Molnar M; Romero R; Hertelendy F

- SO AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, (1993 Oct) 169 (4) 825-9.
Journal code: 0370476. ISSN: 0002-9378.
- AB OBJECTIVE: Our aim was to evaluate the effects of the cytokines interleukin-1 and tumor necrosis factor on arachidonic acid release in human myometrial cells. STUDY DESIGN: Primary monolayer cultures of human myometrial cells prelabeled with tritiated arachidonic acid were exposed to interleukin-1 or tumor necrosis factor for varying periods and the release of tritiated arachidonic acid and its loss from phospholipids were measured by radiochromatography. To gain some information on the biologic action of interleukin-1 the contractile response to oxytocin was measured in myometrial strips preincubated with this cytokine. Data were statistically evaluated with analysis of variance or Student's test. RESULTS: Both cytokines caused a dose-dependent increase in tritiated arachidonate release that was suppressed by the protein synthesis inhibitor cycloheximide. Tritiated arachidonic acid release was maximal after 24 hours of stimulation with interleukin-1. Both interleukin-1 and tumor necrosis factor stimulated the release of the isotopically labeled fatty acid from phosphatidylcholine. In addition, interleukin-1 also increased the loss of arachidonic acid from phosphatidic acid and significantly potentiated the oxytocin-evoked myometrial contractility. CONCLUSIONS: Both interleukin-1 and tumor necrosis factor enhance arachidonic acid release, probably by inducing the synthesis of phospholipase A2 and possibly other enzymes involved in the metabolism of phospholipids. In turn, arachidonic acid itself may act as a second messenger, synergizing with other uterotonic agents, as well as serving as the precursor for prostaglandins and various other bioactive eicosanoids.
- L18 ANSWER 14 OF 16 MEDLINE
- AN 91031815 MEDLINE
- TI The role of interleukin-1 in postmenopausal bone loss.
- AU Pacifici R; Rifas L; McCracken R; Avioli L V
- SO EXPERIMENTAL GERONTOLOGY, (1990) 25 (3-4) 309-16.
Journal code: 0047061. ISSN: 0531-5565.
- AB Interleukin-1 (IL-1), a cytokine best known for its ability to stimulate lymphocyte proliferation, has recently been shown to stimulate bone resorption and modulate bone formation in vivo. Consequently, the authors have devised a series of studies to investigate the relationship between bone remodeling, menopause, and monocyte IL-1-secretion. In a first study, monocytes from osteoporotic patients were found to produce more IL-1 than monocytes from control subjects. IL-1 activity was also found to reflect histomorphometric indices of bone formation, but not of bone resorption. In a second study, devised to assess the effect of menopause on the relationship between IL-1 and bone turnover, a significant correlation was found between IL-1 and BGP in premenopausal osteoporotic women and osteoporotic men, but not in both postmenopausal osteoporotic subjects and normal subjects of either sex. In a third study, IL-1 from untreated postmenopausal women was found to be higher than in either untreated premenopausal or estrogen/progesterone-treated postmenopausal women. A significant negative correlation was found between IL-1 and years since menopause in both the healthy and osteoporotic postmenopausal women. Premenopausal IL-1 levels were achieved within eight years of menopause in the healthy but not in the osteoporotic subjects. In osteoporotic women, high IL-1 levels were evident as long as 15

09/632657

years after menopause. IL-1 also correlated inversely with mineral density as measured by quantitative computer tomography. In prospective study, treatment with estrogen/progesterone caused a significant increase in IL-1 activity. This data indicates that monocyte IL-1 production mirrors the rate of bone turnover in both the healthy and osteoporotic patient, and that alteration in IL-1 production may underlie the postmenopausal acceleration of bone loss and its inhibition by ovarian steroids.

L18 ANSWER 15 OF 16 MEDLINE
AN 89184634 MEDLINE
TI Ovarian steroid treatment blocks a postmenopausal increase in blood monocyte interleukin 1 release.
AU Pacifici R; Rifas L; McCracken R; Vered I; McMurtry C; Avioli L V; Peck W A
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1989 Apr) 86 (7) 2398-402.
Journal code: 7505876. ISSN: 0027-8424.

AB In previous studies, we showed that blood monocyte elaboration of interleukin 1 (IL-1), a known stimulator of bone resorption, was higher in osteoporotic patients with rapid bone turnover than in those with slow turnover and in nonosteoporotic subjects. Since an acceleration of bone loss following menopause contributes to the risk of osteoporosis in women, we have studied the effects of menopause and ovarian steroid treatment on IL-1 release by monocytes obtained from nonosteoporotic and osteoporotic women. IL-1 activity in the monocyte culture medium derived from untreated postmenopausal women (nonosteoporotic and osteoporotic) was higher than in the medium derived from either untreated premenopausal or estrogen/progesterone-treated postmenopausal women. A significant negative correlation was found between IL-1 and years since menopause in both the healthy ($r = -0.75$; P less than 0.005) and the osteoporotic ($r = -0.61$; P less than 0.01) untreated postmenopausal women. The difference between the two slopes was significant at P less than 0.05. Premenopausal IL-1 levels were achieved within 8 years of menopause in the nonosteoporotic, but not in the osteoporotic, subjects in whom increases were evident as long as 15 years after menopause. IL-1 also correlated inversely with vertebral mineral density ($r = -0.37$; P less than 0.05), as measured by quantitative computed tomography. In prospective studies, treatment with estrogen/progesterone for 1 month caused a substantial highly significant decrease in IL-1 activity in each of three nonosteoporotic and five osteoporotic women, confirming the apparent effect of hormone therapy observed in the cross-sectional analysis. Although a cause-effect relationship has not been established, it is our hypothesis, based on these data, that alterations in IL-1 production may underlie the postmenopausal acceleration in bone loss and its inhibition by ovarian steroids. Persistent elevation of IL-1 secretion appears to be a feature of postmenopausal osteoporosis.

L18 ANSWER 16 OF 16 MEDLINE
AN 89139743 MEDLINE
TI Effects of estrogen in vivo and in vitro on spontaneous interleukin-1 release by monocytes from postmenopausal women.
AU Stock J L; Coderre J A; McDonald B; Rosenwasser L J
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1989 Feb) 68 (2) 364-8.
Journal code: 0375362. ISSN: 0021-972X.

Searcher : Shears 308-4994

09/632657

AB Estrogen (E) inhibits bone resorption, but the mechanism of this effect is unknown. Interleukin-1 (IL-1) stimulates bone resorption in vitro and may be produced in bone by mononuclear phagocytes. Recently, the spontaneous release of IL-1 from peripheral monocytes was found to reflect bone formation in a subset of patients with idiopathic osteoporosis. We suspected that the action of E on bone is mediated indirectly by its effect on monocyte IL-1 activity. Eleven normal postmenopausal women taking no medications were given conjugated E (0.625 mg daily) for 3-9 weeks. Supernatants from cultured peripheral monocytes were analyzed for IL-1 production by stimulation of a cloned murine helper T-cell line. IL-1 release was expressed as a percentage of maximum release corrected for monocyte number. IL-1 release before E treatment was $11.0 \pm 0.2\%$ (\pm SE), it was $7.8 \pm 1.6\%$ after E treatment ($P = \text{NS}$). IL-1 release fell in each of the three women with the highest initial values (46% to 5%, 25% to 17%, and 18% to 12%). IL-1 release did not correlate with serum osteocalcin or fasting urinary calcium either before or after E treatment. Addition of 10^{-7} - 10^{-10} mol/L 17 beta-estradiol to cultured monocytes obtained before E treatment caused an increase in IL-1 release that did not follow a dose-response relationship. Treatment of postmenopausal women with E did not affect spontaneous IL-1 release by peripheral monocytes in vitro. The addition of E in vitro did not produce consistent changes in IL-1 release by these cells. This does not exclude the possibility that E may affect monocyte IL-1 release in subsets of women with high spontaneous monocyte IL-1 release with or without osteoporosis.

(FILE 'HCAPLUS' ENTERED AT 15:36:06 ON 18 JUL 2002)

L5 2 SEA FILE=REGISTRY ABB=ON PLU=ON "INTERLEUKIN-1B
CONVERTING ENZYME (HUMAN ISOLATE 1 YEAR OLD MALE CELL
LINE THP.1 - ACUTE MONOCYTIC LEUKEMIA)"/CN
L6 101 SEA FILE=REGISTRY ABB=ON PLU=ON INTERLEUKIN 1 ?/CN
L7 126 SEA FILE=REGISTRY ABB=ON PLU=ON "INTERLEUKIN-1"/CN
L8 216 SEA FILE=REGISTRY ABB=ON PLU=ON L5 OR L6 OR L7
L19 40718 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR (INTERLEUKIN OR
IL)(W)(1A OR 1ALPHA OR 1 OR 1B OR 1BETA OR 1A OR 1ALPHA
OR 1B OR 1BETA OR 1RN OR 1RN) OR IL1A? OR IL1B? OR IL1A?
OR IL1B? OR IL1RN OR IL1RN OR IL1
L20 102 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND (PREMENOPAUS?
OR PERIMENOPAUS? OR MENOPAUS? OR "CHANGE OF LIFE")
L21 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L20 AND (MUTAT? OR
MUTANT? OR MUTAGEN? OR POLYMORPH? OR POLY MORPH? OR
(VARIAT? OR VARIANT) (5A) ALLEL?)

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L22 0 L21 NOT (L2 OR L12)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
JICST-EPLUS, JAPIO' ENTERED AT 15:38:34 ON 18 JUL 2002)

L23 20 S.L21
L24 2 S L23 NOT L13
L25 2 DUP REM L24 (0 DUPLICATES REMOVED)

L25 ANSWER 1 OF 2 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:247140 SCISEARCH
THE GENUINE ARTICLE: 409VA
TITLE: Sex steroids and bone
AUTHOR: Compston J E (Reprint)

Searcher : Shears 308-4994

09/632657

CORPORATE SOURCE: Addenbrookes Hosp, Dept Med, Level 5, Box 157,
Cambridge CB2 2QQ, England (Reprint); Univ
Cambridge, Sch Clin Med, Dept Med, Cambridge,
England
COUNTRY OF AUTHOR: England
SOURCE: PHYSIOLOGICAL REVIEWS, (JAN 2001) Vol. 81, No. 1,
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ISSN: 0031-9333.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 417

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Sex steroids are essential for skeletal development and the maintenance of bone health throughout adult life, and estrogen deficiency at **menopause** is a major pathogenetic factor in the development of osteoporosis in postmenopausal women. The mechanisms by which the skeletal effects of sex steroids are mediated remain incompletely understood, but in recent years there have been considerable advances in our knowledge of how estrogens and, to a lesser extent androgens, influence bone modeling and remodeling in health and disease. New insights into estrogen receptor structure and function, recent discoveries about the development and activity of osteoclasts, and lessons learned from human and animal genetic **mutations** have all contributed to increased understanding of the skeletal effects of estrogen, both in males and females. Studies of untreated and treated osteoporosis in postmenopausal women have also contributed to this knowledge and have provided unequivocal evidence for the potential of high-dose estrogen therapy to have anabolic skeletal effects. The development of selective estrogen receptor modulators has provided a new approach to the prevention of osteoporosis and other major diseases of **menopause** and has implications for the therapeutic use of other steroid hormones, including androgens. Further elucidation of the mechanisms by which sex steroids affect bone thus has the potential to improve the clinical management not only of osteoporosis, both in men and women, but also of a number of other diseases related to sex hormone status.

L25 ANSWER 2 OF 2 SCISEARCH COPYRIGHT 2002 ISI (R)

ACCESSION NUMBER: 96:779075 SCISEARCH

THE GENUINE ARTICLE: VN326

TITLE: INFLUENCE OF VITAMIN-D-RECEPTOR GENOTYPE ON BONE
MASS CHANGES AFTER RENAL-TRANSPLANTATION

AUTHOR: TORRES A (Reprint); MACHADO M; CONCEPCION M T;
MARTIN N; LORENZO V; HERNANDEZ D; RODRIGUEZ A P;
RODRIGUEZ A; DEBONIS E; GONZALEZPOSADA J M;
HERNANDEZ A; SALIDO E

CORPORATE SOURCE: UNIV HOSP, SERV NEFROL, OFRA S-N, LA LAGUNA 38320,
TENERIFE, SPAIN (Reprint); UNIV LA LAGUNA, HOSP UNIV
CANARIAS, SERV NEFROL, TENERIFE, SPAIN; UNIV LA
LAGUNA, HOSP UNIV CANARIAS, SERV RADIODIAGNOST,
TENERIFE, SPAIN; UNIV LA LAGUNA, HOSP UNIV CANARIAS,
UNIDAD INVEST, TENERIFE, SPAIN

COUNTRY OF AUTHOR: SPAIN

SOURCE: KIDNEY INTERNATIONAL, (NOV 1996) Vol. 50, No. 5, pp.
1726-1733.

Searcher : Shears 308-4994

09/632657

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 37

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Renal transplant patients immunosuppressed with cyclosporine A (CsA) exhibit both a significant bone loss and an increased rate of bone fractures. An association between common **allelic variants** of the the vitamin D receptor (VDR) gene and bone mineral density and turnover has been reported in adults. However, the genetic influence on the rate of bone loss after renal transplantation has not been explored. We prospectively determined the changes in spinal mineral density in 34 consecutive nondiabetic adults who received a cadaveric renal allograft. Serum biochemical markers of bone metabolism and the vertebral mineral density (VMD) assessed by quantitative computed tomography were determined at the time of transplantation and three and twelve months later. In fifteen patients the histomorphometric features of **iliac** bone were analyzed at baseline and twelve months after transplantation. VDR alleles were typed by a PCR assay based on a **polymorphic** BsmI restriction site. Patients with the so-called 'favorable' bb genotype (N = 12) were compared with those with the Bb or BB genotype (N = 22). Baseline VMD was similar in patients with or without the favorable bb genotype. Three months after transplantation the mean (+/- SD) VMD decreased 14 +/- 13.3 percent in all patients (16.5 +/- 13.1% in patients homozygous for the b allele and 13.77 +/- 13.9% in those with Bb or BB genotypes). The rate of VMD loss at this time inversely correlated with pretransplant PTH levels ($r = -0.40$; $P < 0.05$). Between 3 and 12 months after transplantation, patients with the favorable bb genotype recovered more VMD than those with Bb or BB types and showed a significantly higher Z score at the end of the follow-up (-0.37 ± 1.16 vs. -1.10 ± 1.20 , respectively; $P < 0.05$). The beneficial effect of bb genotype was independent of the prevailing PTH levels and was also observed in those patients with a baseline PTH level < 250 pg/ml (final Z score: bb, -0.42 ± 1.3 , N = 11; Bb/BB, -1.35 ± 0.8 , N = 11, $P < 0.05$). At the end of follow-up, the histomorphometric studies shelled a higher bone formation rate adjusted for PTH levels in patients with the Bb or BB genotype than in those with the favorable bb genotype (0.29 ± 0.06 vs. 0.21 ± 0.08 $\mu\text{m}^3/\mu\text{m}^2/\text{day}$ respectively; $P < 0.05$). In conclusion, high pretransplant PTH levels enhance the early trabecular bone loss after renal transplantation, and functionally different alleles of the vitamin D receptor gene may condition the bone turnover and the degree of recovery of the bone mass.

(FILE 'HCAPIUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:40:35 ON 18 JUL 2002)

L26 1414 S DUFF G?/AU
L27 501 S KORNMAN K?/AU
L28 147 S VAN DIJK S?/AU
L29 0 S L26 AND L27 AND L28
L30 42 S L26 AND (L27 OR L28)
L31 0 S L27 AND L28
L32 4 S (L30 OR L26 OR L27 OR L28) AND L20
L33 3 DUP REM L32 (1 DUPLICATE REMOVED)

- Author(s)

09/632657

L33 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:168192 HCAPLUS
DOCUMENT NUMBER: 134:217981
TITLE: Genetic techniques for determining genotype of
IL-1 gene cluster (IL-1A, IL-1B and IL-1RN genes) in females, and their use in determining susceptibility of female to developing osteoporosis
INVENTOR(S): Van Dijk, Simon; Duff, Gordon W.
PATENT ASSIGNEE(S): Interleukin Genetics, Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016377	A2	20010308	WO 2000-US23844	20000830
WO 2001016377	A3	20020117		
W: AE, AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, TR, US, YU, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
BR 2000014150	A	20020514	BR 2000-14150	20000830
EP 1212464	A2	20020612	EP 2000-961425	20000830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				

PRIORITY APPLN. INFO.: US 1999-151460P P 19990830
WO 2000-US23844 W 20000830

AB The invention provides mol. genetic techniques for detg. the genotype of the IL-1 gene cluster (IL-1A, IL-1B and IL-1RN genes) in females, in order to det. the susceptibility of a female to developing osteoporosis. The invention relates that gene IL-1A encodes interleukin 1.alpha., gene IL-1B encodes interleukin 1.beta., while gene IL-1RN encodes interleukin 1 receptor antagonist. The invention provides that the IL-1A, IL-1B and IL-1RN alleles can be detecting using: (1) allele-specific hybridization; (2) DNA sequencing of a portion of the allele; (3) electrophoresis mobility of allele or fragments generated using a restriction endonuclease; (4) single-stranded conformation polymorphism; (5) oligonucleotide ligation assay, or (6) primer specific extension. The invention also relates that the alleles may be subjected to an amplification step prior to the detection steps listed above. The invention further relates that females contg. allele 2 of IL-1A, allele 2 of IL-1B (3954), allele 1 of IL-1B (-511), and allele 1 of IL-1RN (haplotype 1) are susceptible to larger bone loss and/or increased risk of fractures during the early menopausal years. Still further, the invention relates that females contg. allele 1 of IL-1A, allele 1 of IL-1B (3954), allele 2

Searcher : Shears 308-4994

09/632657

of **IL-1B** (-511) and allele 2 of **IL-1RN** (haplotype 2) are susceptible to larger bone loss and/or increased risk of fractures during post-menopause. The invention also provides a method for screening test compds. to identify therapeutics for osteoporosis, wherein the therapeutics are modulators (antagonists or agonists) of **IL-1** activity. The invention further provides for the use of identified therapeutic in treatment and/or prevention of osteoporosis. Finally, the invention provides a method for detg. the effectiveness of therapeutic in a subject who has or is predisposed to developing osteoporosis.

L33 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:437912 BIOSIS
DOCUMENT NUMBER: PREV200000437912
TITLE: **IL-1** receptor antagonist gene
polymorphism associated with age of **menopause**

AUTHOR(S): **van Dijk, S. (1)**; Stone, K. L.; Hannon, R. A.; Lui, L. L.; Sorrell, J. A.; Eastell, R.; Cummings, S. R.; **Duff, G. W.**
CORPORATE SOURCE: (1) Interleukin Genetics, Inc., San Antonio, TX USA
SOURCE: Journal of Bone and Mineral Research, (September, 2000) Vol. 15, No. Suppl. 1, pp. S537. print.
Meeting Info.: Twenty-Second Annual Meeting of the American Society for Bone and Mineral Research Toronto, Ontario, Canada September 22-26, 2000
American Society for Bone and Mineral Research
. ISSN: 0884-0431.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L33 ANSWER 3 OF 3 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:886548 SCISEARCH
THE GENUINE ARTICLE: 346YJ
TITLE: **IL-1** receptor antagonist gene
polymorphism associated with age of **menopause**.

AUTHOR: vanDijk S (Reprint); Stone K L; Hannon R A; Lui L L; Sorrell J A; Eastell R; Cummings S R; **Duff G W**

CORPORATE SOURCE: INTERLEUKIN GENET INC, SAN ANTONIO, TX; UNIV CALIF SAN FRANCISCO, SAN FRANCISCO, CA 94143; UNIV SHEFFIELD, SHEFFIELD, S YORKSHIRE, ENGLAND

COUNTRY OF AUTHOR: USA; ENGLAND
SOURCE: JOURNAL OF BONE AND MINERAL RESEARCH, (SEP 2000)
Vol. 15, Supp. [1], pp. M341-M341.
Publisher: AMER SOC BONE & MINERAL RES, 2025 M ST, N W, STE 800, WASHINGTON, DC 20036-3309.
ISSN: 0884-0431.

DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 0

L34

41 S VANDIJK S?/AU

Searcher : Shears 308-4994

09/632657

L35 1 S L34 AND L20
L36 0 S L35 NOT L32

FILE 'HOME' ENTERED AT 15:45:02 ON 18 JUL 2002

Searcher : Shears 308-4994

GenCore version 4.5
Copyright (c) 1993 - 2000 Compugen Ltd.

OM nucleic - nucleic search, using sw model

Run on: July 18, 2002, 02:34:11 ; Search time 1918.6 Seconds
(without alignments)
218.144 Million cell updates/sec

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Perfect score: 20
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Scoring table: IDENTITY_NUC
Gapop 10.0 , Gapext 1.0

Searched: 1797656 seqs, 10463268293 residues

Total number of hits satisfying chosen parameters: 3595112

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database :

GenEmbl.*

- 1: gb.ba.*
- 2: gb.htg.*
- 3: gb.in.*
- 4: gb.om.*
- 5: gb.ov.*
- 6: gb.pat.*
- 7: gb.ph.*
- 8: gb.pl.*
- 9: gb.pr.*
- 10: gb.ro.*
- 11: gb.srs.*
- 12: gb.sy.*
- 13: gb.un.*
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- 15: em.ba.*
- 16: em.fun.*
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- 18: em.in.*
- 19: em.mu.*
- 20: em.om.*
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- 22: em.ov.*
- 23: em.pat.*
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- 27: em.sts.*
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- 32: em.htg_other.*
- 33: em.htg_inv.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

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2	20	100.0	20	6	AX052810	Sequence
3	20	100.0	20	6	AX067270	Sequence
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6	20	100.0	142432	5	AC017074	Homo sapi
7	20	100.0	145465	2	AC069399	Homo sapi
8	20	100.0	185276	2	AC104653	Homo sapi
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ALIGNMENTS

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DEFINITION	AX015634					
ACCESSION	AX015634.1	GI:10041463				
VERSION						
KEYWORDS						
SOURCE		Synthetic construct.				
ORGANISM		artificial sequence.				
REFERENCE		1 (bases 1 to 20)				
AUTHORS		Blattacharya S., Leaves N., Cockson W.O. and McFatt M.F.				
TITLE		Polymorphism i: linkage of asthma to a locus on chromosome 2				
JOURNAL		Patent: WO 9950451-A 9 07-OCT-1999;				
		Blattacharya SUMIT (GB); ISIS INNOVATION (GB); LEAVES NICHOLAS				
		(GB); COCKSON WILLIAM OSWOND CHARLES (GB); MCFATT MIRIAM FLEUR				
		(GB)				

FEATURES

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Bao.W., Sun.Y., Wu.Q., Wang.H., Yang.X., Cheng.C., Wang.Y., Niu.Y., Qi.X., Li.T., Zhang.H., Liu.N., Wu.D., Yu.B., Fan.H., Liu.Y., Li.G., Li.C., Bao.Q., Bao.J., Wang.X., Song.L., Zhang.L., Guo.D., Huang.F., Zhang.G., Li.J., Bian.X., Zhang.M., Li.L., Feng.X., Yu.J. and Yang.H.

Chromosome 3p genomic sequence

JOURNAL

REFERENCE

AUTHORS

Unpublished

2 (bases 1 to 125685)

Wang.J., Hu.S., Dong.W., Wang.J., Zhang.Y., Zhang.H., Liu.B., Bao.W., Sun.Y., Wu.Q., Wang.H., Yang.X., Cheng.C., Wang.Y., Niu.Y., Qi.X., Li.T., Zhang.H., Liu.N., Wu.D., Yu.B., Fan.H., Liu.Y., Li.G., Li.C., Bao.Q., Bao.J., Wang.X., Song.L., Zhang.L., Guo.D., Huang.F., Zhang.G., Li.J., Bian.X., Zhang.M., Li.L., Feng.X., Yu.J. and Yang.H.

Direct Submission

Submitted (23-MAY-2000) Human Genomic Center, Institute of Genetics, Chinese Academy of Sciences, Datun Road, Beijing, Beijing 100101, P.R.China

COMMENT

* NOTE: This is a 'working draft' sequence. It currently consists of 31 contigs. The true order of the pieces is not known and their order in this sequence record is arbitrary. Gaps between the contigs are represented as runs of N, but the exact sizes of the gaps are unknown. This record will be updated with the finished sequence as soon as it is available and the accession number will be preserved.

1 2046: contig of 2046 bp in length
 2047 gap of unknown length
 4344: contig of 2298 bp in length.
 4345 gap of unknown length
 7596: contig of 3252 bp in length.
 7597 gap of unknown length.
 10313: contig of 2717 bp in length
 10314 gap of unknown length
 12296: contig of 1983 bp in length
 12297 gap of unknown length
 15201: contig of 2905 bp in length
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FEATURES

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 DEFINITION Homo sapiens BAC clone RP11-432G15 from 2, complete sequence.
 ACCESSION AC017074
 VERSION AC017074.9 GI:18093142
 KEYWORDS HIG.
 SOURCE human.

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Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE

1 (bases 1 to 142432)
 Sulston, J.E. and Waterston, R.
 Toward a complete human genome sequence
 Genome Res. 8 (11), 1097-1109 (1998)

JOURNAL

MEDLINE

REFERENCE

2 (bases 1 to 142432)
 Pearman, C., Haakenson, W., Dignau, G. and Dixon, R.
 The sequence of Homo sapiens BAC clone RP11-432G15
 Unpublished (2001)

JOURNAL

AUTHORS

TITLE

REFERENCE

JOURNAL

AUTHORS

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REFERENCE

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JOURNAL

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SOURCE human.
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominoidea; Homo.
REFERENCE
1 (bases 1 to 145465)
AUTHORS
Bao,J., Bao,Q., Bao,W., Bian,X., Cao,T., Chen,C., Chen,J., Ding,H.,
Dong,W., Fan,H., Feng,X., Guan,Q., Gu,X., Guo,D., He,L., Hu,S.,
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Luo,J., Niu,Y., Qi,Q., Qi,X., Song,S., Sun,M., Sun,W., Sun,Y.,
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Zhang,L., Zhang,M., Zhang,X., Zhang,X., Zhang,Y., Zhang,Y.,
Zhang,Z., Zhu,B., Yu,J. and Yang,H.
Unpublished
Chromosome 3p genomic sequence
2 (bases 1 to 145465)
AUTHORS
Bao,J., Bao,Q., Bao,W., Bian,X., Cao,T., Chen,C., Chen,J., Ding,H.,
Dong,W., Fan,H., Feng,X., Guan,Q., Gu,X., Guo,D., He,L., Hu,S.,
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Luo,J., Niu,Y., Qi,Q., Qi,X., Song,S., Sun,M., Sun,W., Sun,Y.,
Tao,R., Wang,H., Wang,J., Wang,J., Wang,L., Wang,L., Wang,R.,
Wang,X., Wang,X., Wang,Y., Wu,D., Wu,Q., Xie,F., Xuan,Z., Xue,Y.,
Yan,C., Yang,X., Yu,B., Zeng,Y., Zhang,G., Zhang,H., Zhang,H.,
Zhang,L., Zhang,M., Zhang,X., Zhang,X., Zhang,Y., Zhang,Y.,
Zhang,Z., Zhu,B., Yu,J. and Yang,H.
Direct Submission
Submitted (29-MAY-2000) Human Genomic Center, Institute of
Genetics, Chinese Academy of Sciences, Datun Road, Beijing, Beijing
100101, P. R. China
COMMENT
On Sep 27, 2000 this sequence version replaced gi:8101158.
-----Genome Center
Center:Beijing Center
Center code:Beijing
Website:http://hgsc.lgtp.ac.cn
http://www.genomics.org.cn

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Contact:hgsc@lgt.ac.cn
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Center project name:14 project
Center clone name: RP11-348L20
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Chemistry: Dye-terminator; ET 55% of reads
Assembly program: Phrap; version 0.950329
Consensus quality: 117063 bases at least Q40
Consensus quality: 131502 bases at least Q30
Consensus quality: 142408 bases at least Q20
Insert size: 103473; sum-of-contigs
Quality coverage: 3.19x in Q20 bases;sum-of-contigs
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* NOTE: This is a 'working draft' sequence. It currently
* consists of 46 contigs. The true order of the pieces
* is not known and their order in this sequence record is
* arbitrary. Gaps between the contigs are represented as
* runs of N, but the exact sizes of the gaps are unknown.
* This record will be updated with the finished sequence.
* as soon as it is available and the accession number will
* be preserved.
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* 1323 1422: gap of unknown length
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* 4783 4882: gap of unknown length
* 4883 6515: contig of 1633 bp in length
* 6516 6615: gap of unknown length
* 6616 8247: contig of 1632 bp in length
* 8248 8348: gap of unknown length
* 8349 10115: contig of 1768 bp in length
* 10116 10215: gap of unknown length
* 10216 11673: contig of 1464 bp in length
* 11674 11773: gap of unknown length
* 11774 13991: contig of 2212 bp in length
* 13992 14091: gap of unknown length
* 14092 16303: contig of 2212 bp in length
* 16304 16404: gap of unknown length
* 16405 18584: contig of 2181 bp in length
* 18585 18684: gap of unknown length
* 18685 20414: contig of 1729 bp in length
* 20415 20513: gap of unknown length
* 20514 23870: contig of 3357 bp in length
* 23871 23970: gap of unknown length
* 23971 27418: contig of 3448 bp in length
* 27419 27518: gap of unknown length
* 27519 30640: contig of 3122 bp in length
* 30641 30741: gap of unknown length
* 30742 33893: contig of 3153 bp in length
* 33894 33993: gap of unknown length
* 33994 37523: contig of 3530 bp in length
* 37524 37624: gap of unknown length
* 37625 40649: contig of 3026 bp in length
* 40650 40750: gap of unknown length
* 40751 44869: contig of 4120 bp in length
* 44870 44969: gap of unknown length
* 44970 48734: contig of 3765 bp in length
* 48735 48835: gap of unknown length
* 48836 50049: contig of 1215 bp in length
* 50050 50149: gap of unknown length
* 50150 54117: contig of 4168 bp in length
* 54118 54318: gap of unknown length
* 54319 58377: contig of 3960 bp in length
* 58378 58477: gap of unknown length
* 58478 64659: contig of 6182 bp in length
* 64660 64759: gap of unknown length
* 64760 70948: contig of 6187 bp in length
* 70949 71048: gap of unknown length
* 71049 77313: contig of 6267 bp in length
* 77314 77414: gap of unknown length
* 77415 83013: contig of 5599 bp in length
* 83014 83113: gap of unknown length
* 83114 89398: contig of 6286 bp in length
* 89399 89498: gap of unknown length
* 89499 96428: contig of 6930 bp in length
* 96429 96528: gap of unknown length
* 96529 105237: contig of 8709 bp in length
* 105238 105338: gap of unknown length
* 105339 111440: contig of 6103 bp in length
* 111441 121258: gap of unknown length
* 121259 121359: contig of 9718 bp in length
* 121360 130423: contig of 9055 bp in length
* 130424 130523: gap of unknown length
* 130524 140609: contig of 10086 bp in length
* 140610 140709: gap of unknown length
* 140710 161114: contig of 20405 bp in length
* 161115 161215: gap of unknown length
* 161216 185276: contig of 24062 bp in length.

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FEATURES

```

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1. .185276
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/db_xref="taxon:9606"
/chromosome="2"
/clone="RP11-295D2"
1. .1390
/note="assembly_name:Contig22"
misc_feature
1491. .3004
misc_feature

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/note="assembly_name:Contig24"
3105. .4782
/note="assembly_name:Contig27"
4883. .6515
/note="assembly_name:Contig28"
6616. .8247
/note="assembly_name:Contig29"
8348. .10115
/note="assembly_name:Contig30"
10216. .11673
/note="assembly_name:Contig31"
11780. .13991
/note="assembly_name:Contig32"
14092. .16303
/note="assembly_name:Contig33"
16404. .18584
/note="assembly_name:Contig34"
18685. .20413
/note="assembly_name:Contig35"
clone_end:T7
vector_side:left"
20514. .23870
/note="assembly_name:Contig36"
23971. .27418
/note="assembly_name:Contig37"
27519. .30640
/note="assembly_name:Contig38"
30741. .33893
/note="assembly_name:Contig39"
33994. .37523
/note="assembly_name:Contig40"
37624. .40649
/note="assembly_name:Contig41"
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vector_side:left"
40750. .44869
/note="assembly_name:Contig42"
44970. .48734
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48835. .50049
/note="assembly_name:Contig44"
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/note="assembly_name:Contig46"
58478. .64659
/note="assembly_name:Contig47"
64760. .70948
/note="assembly_name:Contig48"
71047. .77313
/note="assembly_name:Contig49"
77414. .83012
/note="assembly_name:Contig50"
83113. .89398
/note="assembly_name:Contig51"
89499. .96428
/note="assembly_name:Contig52"
96529. .105237
/note="assembly_name:Contig53"
105338. .111440
/note="assembly_name:Contig54"
111541. .121258
/note="assembly_name:Contig55"
121359. .130423
/note="assembly_name:Contig56"
130524. .140609
/note="assembly_name:Contig57"
140710. .161114
/note="assembly_name:Contig58"
161215. .185276
/note="assembly_name:Contig59"

```

```

BASE COUNT 55292 a 37754 c 36132 g 52691 t 3407 others
ORIGIN

```

Smit, A.F.A. & Green, P. (1996-1997)
<http://ftp.genome.washington.edu/RM/RepeatMasker.html>
 ----- Genome Center
 Center: Whitehead Institute/ MIT Center for Genome Research
 Center code: WIBR
 Web site: <http://www-seq.wi.mit.edu>
 Contact: sequence_submissions@genome.wi.mit.edu
 ----- Project Information
 Center project name: L7064
 Center clone name: 362.L_21

* NOTE: This record contains 86 individual
 * sequencing reads that have not been assembled into
 * contigs. Runs of N are used to separate the reads
 * and the order in which they appear is completely
 * arbitrary. Low-pass sequence sampling is useful for
 * identifying clones that may be gene-rich and allows
 * overlap relationships among clones to be deduced.
 * However, it should not be assumed that this clone
 * will be sequenced to completion. In the event that
 * the record is updated, the accession number will
 * be preserved.

1
 * 651: contig of 651 bp in length
 * 652 751: gap of 100 bp
 * 752 1406: contig of 655 bp in length
 * 1407 1506: gap of 100 bp
 * 1507 2175: contig of 665 bp in length
 * 2176 2275: gap of 100 bp
 * 2276 2970: contig of 695 bp in length
 * 2971 3070: gap of 100 bp
 * 3071 3729: contig of 655 bp in length
 * 3730 3829: gap of 100 bp
 * 3830 4461: contig of 632 bp in length
 * 4462 4561: gap of 100 bp
 * 4562 5221: contig of 660 bp in length
 * 5222 5321: gap of 100 bp
 * 5322 5984: contig of 663 bp in length
 * 5985 6084: gap of 100 bp
 * 6085 6755: contig of 671 bp in length
 * 6756 6855: gap of 100 bp
 * 6856 7542: contig of 667 bp in length
 * 7543 7642: gap of 100 bp
 * 7643 8303: contig of 661 bp in length
 * 8304 8403: gap of 100 bp
 * 8404 9073: contig of 670 bp in length
 * 9074 9173: gap of 100 bp
 * 9174 9825: contig of 652 bp in length
 * 9826 9925: gap of 100 bp
 * 9926 10641: contig of 716 bp in length
 * 10642 10741: gap of 100 bp
 * 10742 11434: contig of 693 bp in length
 * 11435 11534: gap of 100 bp
 * 11535 12216: contig of 682 bp in length
 * 12217 12316: gap of 100 bp
 * 12317 12967: contig of 651 bp in length
 * 12968 13067: gap of 100 bp
 * 13068 13716: contig of 649 bp in length
 * 13717 13816: gap of 100 bp
 * 13817 14487: contig of 671 bp in length
 * 14488 14587: gap of 100 bp
 * 14588 15250: contig of 663 bp in length
 * 15251 15350: gap of 100 bp
 * 15351 16062: contig of 712 bp in length
 * 16063 16162: gap of 100 bp
 * 16163 16839: contig of 677 bp in length
 * 16840 16939: gap of 100 bp
 * 16940 17611: contig of 672 bp in length
 * 17612 17711: gap of 100 bp
 * 17712 18352: contig of 641 bp in length
 * 18353 18452: gap of 100 bp
 * 18453 19151: contig of 699 bp in length
 * 19152 19251: gap of 100 bp
 * 19252 19958: contig of 707 bp in length

* 19959 20058: gap of 100 bp
 * 20059 20741: contig of 683 bp in length
 * 20742 20841: gap of 100 bp
 * 20842 21495: contig of 654 bp in length
 * 21496 21595: gap of 100 bp
 * 21596 22222: contig of 627 bp in length
 * 22223 22322: gap of 100 bp
 * 22323 22931: contig of 669 bp in length
 * 22932 23031: gap of 100 bp
 * 23032 23756: contig of 685 bp in length
 * 23757 23856: gap of 100 bp
 * 23857 24524: contig of 668 bp in length
 * 24525 24624: gap of 100 bp
 * 24625 25293: contig of 665 bp in length
 * 25294 25393: gap of 100 bp
 * 25394 26103: contig of 710 bp in length
 * 26104 26203: gap of 100 bp
 * 26204 26849: contig of 646 bp in length
 * 26850 26949: gap of 100 bp
 * 26950 27637: contig of 678 bp in length
 * 27638 27737: gap of 100 bp
 * 27738 28386: contig of 661 bp in length
 * 28387 28486: gap of 100 bp
 * 28487 29152: contig of 664 bp in length
 * 29153 29252: gap of 100 bp
 * 29253 29918: contig of 666 bp in length
 * 29919 30018: gap of 100 bp
 * 30019 30684: contig of 666 bp in length
 * 30685 30784: gap of 100 bp
 * 30785 31451: contig of 667 bp in length
 * 31452 31551: gap of 100 bp
 * 31552 32202: contig of 651 bp in length
 * 32203 32302: gap of 100 bp
 * 32303 32985: contig of 683 bp in length
 * 32986 33085: gap of 100 bp
 * 33086 33811: contig of 726 bp in length
 * 33812 33911: gap of 100 bp
 * 33912 34600: contig of 689 bp in length
 * 34601 34700: gap of 100 bp
 * 34701 35384: contig of 684 bp in length
 * 35385 35484: gap of 100 bp
 * 35485 36164: contig of 680 bp in length
 * 36165 36264: gap of 100 bp
 * 36265 36994: contig of 730 bp in length
 * 36995 37094: gap of 100 bp
 * 37095 37845: contig of 751 bp in length
 * 37846 37945: gap of 100 bp
 * 37946 38600: contig of 655 bp in length
 * 38601 38700: gap of 100 bp
 * 38701 39385: contig of 655 bp in length
 * 39386 39485: gap of 100 bp
 * 39486 40104: contig of 649 bp in length
 * 40105 40204: gap of 100 bp
 * 40205 40847: contig of 643 bp in length
 * 40848 40947: gap of 100 bp
 * 40949 41595: contig of 648 bp in length
 * 41596 41695: gap of 100 bp
 * 41696 42389: contig of 674 bp in length
 * 42390 42489: gap of 100 bp
 * 42490 43191: contig of 722 bp in length
 * 43192 43291: gap of 100 bp
 * 43292 43972: contig of 681 bp in length
 * 43973 44072: gap of 100 bp
 * 44073 44729: contig of 657 bp in length
 * 44730 44829: gap of 100 bp
 * 44830 45500: contig of 671 bp in length
 * 45501 45600: gap of 100 bp
 * 45601 46248: contig of 648 bp in length
 * 46249 46348: gap of 100 bp
 * 46349 47009: contig of 661 bp in length
 * 47010 47109: gap of 100 bp
 * 47110 47773: contig of 664 bp in length
 * 47774 47873: gap of 100 bp

COMMENT

Submitted (06-JUN-2000) Masahira Hattori, The Institute of Physiological and Chemical Research (RIKEN), Genomic Sciences Center (GSC), Kitasato Univ., 1-15-1 Kitasato, Sagami-hara, Kanagawa 228-8555, Japan (E-mail:hattori@gsc.riken.go.jp,
URL: <http://nsp-gsc.riken.go.jp/>, Tel:81-42-778-5923, Fax:81-42-778-5924

Center: RIKEN Genomic Sciences Center (GSC)

```

Center code: KINEN
Web site: http://tsp.gsc.riken.go.jp/
Contact: hattori@tsp.gsc.riken.go.jp
----- Project Information -----
Center project name: HumDrat118
Center clone name: RP11-74917
----- Summary Statistics -----
Sequencing vector: PCR products; 100% of reads
Chemistry: Dye-terminator ET-americn; 100% of reads
Assembly program: Phrap; version 0.950329
Consensus quality: 156364 bases at least Q40
Consensus quality: 161470 bases at least Q30
Consensus quality: 1614021 bases at least Q20
Insert size: 165440; sum-of-contigs
Quality coverage: 5.97x in Q20 bases; sum-of-contigs

```

NOTE: This is a 'working draft' sequence. It currently consists of 22 contigs. The true order of the pieces is not known and their order in this sequence record is arbitrary. Gaps between the contigs are represented as runs N. But the exact sizes of the gaps are unknown. This record will be updated with the finished sequence as soon as it is available and the accession number will be preserved.

	26680	contig	of	26680	bp	in	length
26781	43880	contig	of	17100	bp	in	length
43981	6316	contig	of	17336	bp	in	length
64117	74115	contig	of	15999	bp	in	length
77516	90011	contig	of	12496	bp	in	length
90112	103577	contig	of	12466	bp	in	length
102678	114227	contig	of	9550	bp	in	length
112338	122049	contig	of	9722	bp	in	length
122150	126655	contig	of	4506	bp	in	length
126756	13018	contig	of	5263	bp	in	length
132119	135659	contig	of	4851	bp	in	length
137070	147009	contig	of	5440	bp	in	length
141610	147009	contig	of	5440	bp	in	length
147110	150145	contig	of	3036	bp	in	length
150246	153171	contig	of	2926	bp	in	length
153212	155871	contig	of	2600	bp	in	length
155972	158760	contig	of	2789	bp	in	length
158881	165800	contig	of	2720	bp	in	length
161681	163325	contig	of	1645	bp	in	length
163432	164786	contig	of	1361	bp	in	length
164887	166415	contig	of	1529	bp	in	length
166516	167540	contig	of	1025	bp	in	length

NOTE: This is a working draft record, and its length consists of 22 contigs. The order of the pieces is arbitrary, and their order in this sequence record is arbitrary. Capabilities of contigs are represented as runs of N, but the exact significance is unknown. This record will be dated with the finished sequence as soon as it is available and the accession number will be preserved.

	1	26680:	contig of	26680 bp in length
*	26681	26780:	gap of	100 bp
*	26781	43880:	contig of	17100 bp in length
*	43881	43980:	gap of	100 bp
*	43981	61316:	contig of	17336 bp in length
*	61317	61416:	gap of	100 bp
*	61417	77435:	contig of	13999 bp in length
*	77416	77515:	gap of	100 bp
*	77516	90011:	contig of	12498 bp in length
*	90012	90111:	gap of	100 bp
*	90112	102577:	contig of	12466 bp in length
*	102578	102677:	gap of	100 bp

* 37913 38012: gap of unknown length
 * 38013 114721: contig of 76709 bp in length
 * 114722 114821: gap of unknown length
 * 114822 170481: contig of 55660 bp in length.

FEATURES

source
 1. 170481
 /organism="Homo sapiens"
 /db_xref="taxon:9606"
 /chromosome="16"
 /clone="RP11-46309"
 /clone_lib="RPCI human BAC library 11"
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 ORIGIN
 Query Match 92.0%; Score 18.4; DB 2; Length 170481;
 Best Local Similarity 95.0%; Pred. No. 39;
 Matches 19; Conservative 0; Mismatches 1; Indels 6; Gaps 0;

QY 1 gctgatatcttggtggaaa 20

||||| ||||||| ||||||| |||||||

Db 116586 GCTCATATCTCGGGGGAAA 116605

RESULT 14

AC091151 171707 bp DNA linear HTG 31-11-2001
 LOCUS Homo sapiens chromosome 18 clone RP11-749H17 map 18, *** SEQUENCING
 DEFINITION IN PROGRESS ***, 2 ordered pieces.
 AC091151
 VERSION AC091151.4 GI:16506886
 KEYWORDS HTG; HTGS_PHASE2; HTGS_FULLTOP; HTGS_ACTIVEPIN.
 SOURCE human
 ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 171707)

AUTHORS Birren,B., Linton,L., Nusbaum,C. and Lander,E.

TITLE Homo sapiens chromosome 18, clone RP11-749H17

JOURNAL Unpublished

AUTHORS 2 (bases 1 to 171707)

Birren,B., Linton,L., Nusbaum,C., Lander,E., Allen,N., Anderson,S.,
 Barna,N., Bastien,V., Boguslavsky,L., Boukhaltier,B., Brown,A.,
 Camarata,J., Campopiano,A., Chang,J., Choepel,Y., Collangelo,M.,
 Collins,S., Collamore,A., Cooke,P., Dearellano,K., Dewar,K.,
 Diaz,J.S., Dodge,S., Faro,S., Ferreira,P., FitzHugh,W., Gage,D.,
 Galagan,J., Gardyna,S., Ginde,S., Goyette,M., Graham,L.,
 Grand-Pierre,N., Hagos,B., Heard,A., Horton,L., Huine,W.,
 Iliev,I., Johnson,R., Jones,C., Karatas,A., Lacroque,K.,
 Lamazares,R., Landers,T., Lehoczy,J., Levine,R., Liu,G.,
 MacLean,C., Macdonald,P., Marquis,N., Matthews,C., McCarthy,M.,
 McEwan,P., McKernan,K., McPheters,R., Meldrum,J., Menes,I.,
 Mihova,T., Mlenga,V., Murphy,T., Naylor,J., Nguyen,C., Norio,C.,
 Norman,C.H., O'Connor,T., O'Donnell,P., O'Neill,D., Oliver,J.,
 Peterson,K., Phunkhang,P., Plerre,N., Pollara,V., Raymond,C.,
 Retta,R., Rieback,M., Riley,R., Rise,C., Rogov,P., Roman,J.,
 Rosetti,M., Roy,A., Santos,R., Schauer,S., Schupack,R., Seaman,S.,
 Severy,P., Souney,C., Spencer,B., Stange-Thomann,N.,
 Stojanovic,N., Straus,N., Subramanian,A., Talamas,J., Testaye,S.,
 Theodore,J., Travers,M., Travis,N., Trigliio,J., Vassiliev,H.,
 Viet,R., Vo,A., Wilson,B., Wu,X., Wymann,D., Ye,W.J., Young,S.,
 Zainoun,J., Zembek,L., Zimmer,A. and Zody,M.

Direct Submission

Submitted (01-APR-2001) Whitehead Institute/MIT Center for Genome

Research, 320 Charles Street, Cambridge, MA 02141, USA

On Oct 28, 2001 this sequence version replaced gi:15421950.

All repeats were identified using RepeatMasker:

Smit, A.F.A. & Green, P. (1996-1997)

http://ftp.genome.washington.edu/RM/RepeatMasker.html

----- Genome Center

Center: Whitehead Institute/ MIT Center for Genome Research

Center code: WTR

Web site: http://www-seq.wi.mit.edu

Contact: sequence_submissions@genome.wi.mit.edu
 ----- Project Information
 Center Project name: 113202
 Center clone name: 749_H_17

* NOTE: This is a 'working draft' sequence. It currently
 * consists of 2 contigs. Gaps between the contigs
 * are represented as runs of N. The order of the pieces
 * is believed to be correct as given, however the sizes
 * of the gaps between them are based on estimates that have
 * provided by the submitter.
 * This sequence will be replaced
 * by the finished sequence as soon as it is available and
 * the accession number will be preserved.

* 1 154357: contig of 154357 bp in length
 * 154358 154457: gap of 100 bp
 * 154458 171707: contig of 17250 bp in length.

FEATURES

source

1. 171707
 /organism="Homo sapiens"
 /db_xref="taxon:9606"
 /chromosome="18"
 /map="18"
 /clone="RP11-749H17"
 /clone_lib="RPCI-11 Human Male BAC"

BASE COUNT 48096 a 36903 c 36956 g 48164 t 1586 others
 ORIGIN

Query Match 92.0%; Score 18.4; DB 2; Length 171707;

Best Local Similarity 95.0%; Pred. No. 39;

Matches 19; Conservative 0; Mismatches 1; Indels 6; Gaps 0;

QY 1 gctgatatcttggtggaaa 20

||||| ||||||| ||||||| |||||||

Db 112934 GCTGATCTCGGGGGAAA 112953

RESULT 15

AC007969 195848 bp DNA linear HTG 20-MAY-2001
 LOCUS Homo sapiens chromosome 18 clone RP11-463D17 map 18, WORKING DRAFT
 DEFINITION SEQUENCE, 4 unordered pieces.

AC007969

AC007969.3 GI:14150900

KEYWORDS HTG; HTGS_PHASE1; HTGS_DRAFT; HTGS_FULLTOP.

SOURCE human.

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 195848)

AUTHORS Birren,B., Linton,L., Nusbaum,C. and Lander,E.

TITLE Homo sapiens chromosome 18, clone RP11-463D17

JOURNAL Unpublished

AUTHORS 2 (bases 1 to 195848)

Birren,B., Linton,L., Nusbaum,C., Lander,E., Allen,N., Anderson,M.,
 Baker,J., Baldwin,J., Barna,N., Beckerly,R., Beck,J., Brown,A.,
 Castle,A., Cerny,J., Collangelo,M., Collins,S., Collamore,A.,
 Cooke,P., Dearellano,K., Depayre,E., Devon,K., Dewar,K.,
 Donelan,L., Doyle,M., Ferreira,P., FitzHugh,W., Forrest,C.,
 Funke,K., Gage,D., Galagan,J., Gardyna,S., Gilbert,D., Grant,S.,
 Hagos,B., Heard,A., Horton,L., Howland,J.C., Jones,C., Kam,L.,
 Karatas,A., Lehoczy,J., Lieu,C., Locke,K., Macdonald,P.,
 Marquis,N., McEwan,P., McGurk,A., McKernan,K., McLaughlin,J.,
 Meldrum,J., Mollia,M., Morris,W., Morrow,J., Mchaleckyj,J.,
 Naylor,J., Niloff,M., O'Connor,T., O'Donnell,P., Pavlin,E.,
 Peterson,K., Pollara,V., Riley,R., Roberts,D., Roy,A., Severy,P.,
 Stange-Thomann,N., Stojanovic,N., Stone,C., Subramanian,A.,
 Testaye,S., Torruella-Miller,I., Vassiliev,H., Vo,A., Wagner,A.,
 Wheeler,J., Wu,X., Wymann,D., Ye,W.J. and Zody,M.

Direct Submission

Submitted (08-JUL-1999) Whitehead Institute/MIT Center for Genome

Research, 320 Charles Street, Cambridge, MA 02141, USA

CC coagulation, multiple organ failure, cardiovascular collapse, and death.
 CC It is therefore useful to identify those individuals who are at risk of
 CC developing an exaggerated systemic inflammatory response to septic
 CC stimuli, so that sepsis therapy (e.g. with IL-1 modulators) can be
 CC tailored to the individual's genetic profile. Sequences AA61915-A61928
 CC represent PCR primers which may be used to amplify IL-1 gene cluster
 CC polymorphic loci. Sequences AA61925-A61926 are primers used to amplify
 CC and type the centromere distal polymorphic microsatellite anchor marker
 CC AF087241 which flanks the IL-1 gene cluster.
 XX
 XX Sequence 20 BP; 5 A; 2 C; 7 G; 6 T; 0 other;

Query Match 100.0%; Score 20; DB 21; Length 20;
 Best Local Similarity 100.0%; Pred. No. 0.89; Mismatches 0; Indels 0; Gaps 0;
 Matches 20; Conservative 0;

QY 1 gctgatattctggtgggaaa 20
 |||||
 Db 1 gctgatattctggtgggaaa 20

RESULT 4
 AA237222
 ID AA237222 standard; DNA: 20 BP.

XX AC AA237222;

XX DT 28-JAN-2000 (first entry)

XX DE PCR primer for interleukin-1 genomic locus.

XX KW PCR primer; IL-1; IL-1A; IL-1B; TNFA; interleukin-1; foetus;

XX KW adverse pregnancy outcome; allele detection; low birth weight; LBW;

XX KW pre-term baby; premature baby; tumour necrosis factor-alpha; ss.

XX OS Synthetic.

XX OS Homo sapiens.

XX PN W05954707-A2.

XX PD 28-OCT-1999.

XX PF 21-APR-1999; 99WO-US08794.

XX PR 21-APR-1998; 98US-0082487.

XX PA (REDI-) MEDICAL SCI SYSTEMS INC.

XX PI Korman KS, Offenbacher S, Duff GW;

XX DR WPI; 2000-013279/01.

XX PT Fetal testing for prediction of low birth weight by detecting an
 XX PT interleukin allele -

XX PS Disclosure; Page 33; 78pp; English.

XX CC This sequence is a PCR primer for the interleukin-1 genomic locus.
 CC The invention relates to a method for determining whether a foetus is
 CC predisposed to having an adverse pregnancy outcome by detecting an
 CC interleukin-1A (IL-1A) (+4845) allele 2, an IL-1 (-511) allele 1 or an
 CC allele in linkage disequilibrium with either of these alleles. The method
 CC comprises: (a) obtaining a nucleic acid sample from the subject; and
 CC (b) detecting an IL-1A (+4845) allele 2, an IL-1 (-511) allele 1 or an
 CC allele in linkage disequilibrium with either of these alleles, where
 CC detection of the alleles or an allele in linkage disequilibrium with
 CC them indicates that the fetus is predisposed to an adverse pregnancy
 CC outcome. The method is used to determine whether a fetus is predisposed
 CC to having a low birth weight (LBW). By determining the IL-1 or tumour
 CC necrosis factor-alpha (TNF-A) genotype an appropriate therapeutic, such
 CC as a corticosteroid, antimetabolite, cytotoxic drug, colchicine or
 CC anti-cytokine, can be administered to compensate for the LBW causative

CC functional mutation. An appropriate therapeutic can be used to treat a
 CC subject predisposed to having a LBW baby, especially a pre-term or
 CC premature baby.

XX SQ Sequence 20 BP; 5 A; 2 C; 7 G; 6 T; 0 other;

Query Match 100.0%; Score 20; DB 21; Length 20;
 Best Local Similarity 100.0%; Pred. No. 0.89; Mismatches 0; Indels 0; Gaps 0;
 Matches 20; Conservative 0;

QY 1 gctgatattctggtgggaaa 20
 |||||
 Db 1 gctgatattctggtgggaaa 20

RESULT 5

AAF77857
 ID AAF77857 standard; DNA: 20 BP.

XX AC AAF77857;

XX DT 30-MAY-2001 (first entry)

XX DE Human IL-1 polymorphic marker AF087241 PCR primer #1.

XX KW Human; IL-1; PCR primer; osteoporosis; interleukin; haplotype pattern;
 XX KW polymorphic marker; microsatellite marker; AF087241; ss.

XX OS Homo sapiens.

XX OS W0200116377-A2.

XX PD 08-MAR-2001.

XX PF 30-AUG-2000; 2000WO-US23844.

XX PR 30-AUG-1999; 99US-0151460.

XX PA (INTE-) INTERLEUKIN GENETICS INC.

XX PI Van Dijk S, Duff GW;

XX DR WPI; 2001-263896/27.

XX PT Determining whether a female is predisposed to the developing
 XX PT osteoporosis involves identifying interleukin-1 haplotype pattern of
 XX PT the female, useful for selecting appropriate osteoporosis therapy

XX PS Disclosure; Page 22; 69pp; English.

XX CC The present invention relates to a method for determining whether a
 XX CC female is predisposed to developing osteoporosis. The method involves
 XX CC identifying the patient's interleukin (IL)-1 haplotype pattern (HP).
 XX CC Presence of HP 1 or HP 2 indicates that the female is susceptible to
 XX CC larger bone loss and/or increased risk of fracture during the early
 XX CC menopausal years (HP 1) or post-menopause (HP 2). The human IL-1 locus
 XX CC genes are flanked by a distal polymorphic marker designated
 XX CC microsatellite anchor marker AF087241. The present sequence is a PCR
 XX CC primer for the AF087241 marker, which was used in the present invention.
 XX SQ Sequence 20 BP; 5 A; 2 C; 7 G; 6 T; 0 other;

Query Match 100.0%; Score 20; DB 22; Length 20;
 Best Local Similarity 100.0%; Pred. No. 0.89; Mismatches 0; Indels 0; Gaps 0;
 Matches 20; Conservative 0;

QY 1 gctgatattctggtgggaaa 20
 |||||
 Db 1 gctgatattctggtgggaaa 20

XX 26-MAY-1999; 990S-0320395.
 PR 01-NOV-1999; 990S-0431352.
 XX (INTE-) INTERLEUKIN GENETICS INC.
 XX Francis SE, Crossman DC, Duff GW, Kornman KS;
 PI WPI: 2001-032066/04.
 DR Diagnosing cardiovascular disease, or susceptibility, using, e.g. for
 XX selecting treatment, from presence of disease-associated allele,
 PI particularly in interleukin-1 genes -
 XX Disclosure: Page 50; 121pp; English.
 PS There is an association of patterns of alleles at four polymorphic loci
 CC in the interleukin-1 (IL-1) gene cluster with cardiovascular disorders.
 CC The present invention relates to a method for the diagnosis of a
 CC cardiovascular disorder (CVD), via detecting a CVD-associated allele in a
 CC patient sample. The method is used to select an appropriate therapy for
 CC CVD, particularly fragile plaque disorder, occlusive disorders or
 CC in-stent restenosis, or a condition associated with a mutation with
 CC linkage disequilibrium with a CVD-associated allele, or to identify risk
 CC factors for CVD, and to formulate a treatment designed to reduce the
 CC risk. The IL-1 gene cluster is found at the 2q13 region of chromosome 2.
 CC IL-1 locus genes are flanked by a centromere proximal polymorphic marker
 CC designated AFM2202e3 at 127.4cM and a distal polymorphic marker
 CC designated AFM087x1 at 127.9cM. The present sequence is a PCR primer
 CC used in the present invention.
 XX Sequence 20 BP; 5 A; 2 C; 7 G; 6 T; 0 other;

Query Match ~ 100.0%; Score 20; DB 22; Length 20;
 Best Local Similarity 100.0%; Pred. No. 0.89;
 Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 gctgatattctggtgggaaa 20
 |||||
 DB 1 gctgatattctggtgggaaa 20

RESULT 9
 AAZ14604/c
 ID AAZ14604 standard; cDNA; 300 BP.
 XX
 AC AAZ14604;
 XX
 DT 12-OCT-1999 (first entry)
 XX
 DE Human gene expression product cDNA sequence SEQ ID NO: 2073.
 XX
 KW Human; gene; gene expression product; diagnosis; therapy; prote;
 KW detection; mapping; tissue typing; profiling; forensic; cancer;
 KW genetic analysis; colorectal cancer; breast cancer; lung cancer; ss.
 XX Homo sapiens.
 OS WO9938972-A2.
 XX
 XX
 PD 05-AUG-1999.
 XX
 XX
 PF 28-JAN-1999; 99WO-US01619.
 XX
 PR 03-APR-1998; 98US-0080666.
 PR 28-JAN-1998; 98US-0072910.
 PR 24-FEB-1998; 98US-0075954.
 PR 31-MAR-1998; 98US-0080114.
 PR 03-APR-1998; 98US-0080515.
 XX
 XX (CHIR) CHIRON CORP.
 PA (HYSE-) HYSEQ INC.

XX Crkventakov R, Dickson M, Drmanac R, Drmanac S;
 PI Escobedo J, Garcia PD, Garcia V, Giese K, Innis MA;
 PI Jones WL, Kassam A, Kennedy GC, Kita D, Labat I;
 PI Lamson G, Leshkowitz D, Pot D, Randazzo F, Reinhard C;
 PI Stache-Crain B, Sudduth-Klinger J, Williams LI;
 XX WPI: 1999-494052/41.
 DR Novel human genes and their expression products which are
 XX differentially expressed in different cell types
 PI Claim 1; Page 1129; 2479pp; English.
 XX
 CC The present invention describes a library of human polynucleotides
 CC comprising the sequences given in AAZ1532 to AAZ1779. Also described is
 CC a method of detecting differentially expressed genes correlated with the
 CC cancerous state of a mammalian cell, comprising detecting at least one
 CC differentially expressed gene product in a test sample from a cell
 CC suspected of being cancerous, where the gene product is encoded by one
 CC of the 5248 polynucleotide sequences given in AAZ1532 to AAZ1779. The
 CC polynucleotides can be used as a source of primers and probes, which can
 CC be used for a variety of purpose, e.g. detection of expression levels,
 CC mapping, tissue typing or profiling, forensics, genetic analysis and
 CC detection of polymorphisms. Polypeptides encoded by the polynucleotides
 CC can be used for raising antibodies for experimental, diagnostic and
 CC therapeutic purposes. The polynucleotides may also be used to construct
 CC arrays for diagnostics (which may be used to determine function of an
 CC encoded protein); and to detect differences in expression levels between
 CC two cells (e.g. to identify abnormal or diseased tissue in a human, to
 CC identify a genetic predisposition or susceptibility to a disease such as
 CC cancer). The polynucleotides of the invention are especially used in the
 CC diagnosis, prognosis and management of colorectal cancer, breast cancer,
 CC and lung cancer. The polynucleotides can also be used to screen for
 CC peptide analogues and antagonists.
 XX Sequence 300 BP; 76 A; 75 C; 70 G; 79 T; 0 other;

Query Match 84.0%; Score 16.8; DB 20; Length 300;
 Best Local Similarity 90.0%; Pred. No. 52;
 Matches 18; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

QY 1 gctgatattctggtgggaaa 20
 |||||
 DB 166 GCIGATATCTAGTGGAAA 147

RESULT 10
 AAS88820
 ID AAS88820 standard; cDNA; 456 BP.
 XX
 AC AAS88820;
 XX
 DT 13-FEB-2002 (first entry)
 XX
 DE DNA encoding novel human diagnostic protein #24624.
 XX
 KW Human; chromosome mapping; gene mapping; gene therapy; forensic;
 KW food supplement; medical imaging; diagnostic; genetic disorder; ss.
 XX Homo sapiens.
 OS WO200175067-A2.
 XX
 XX
 PD 11-OCT-2001.
 XX
 PF 30-MAR-2001; 2001WO-US08631.
 XX
 PR 31-MAR-2000; 2000US-0540217.
 PR 23-AUG-2000; 2000US-0649167.
 XX
 XX (HYSE-) HYSEQ INC.

XX WPI: 2001-639362/73.
 DR P-PSDB: ABG24388.
 XX
 PI New isolated polynucleotide and encoded polypeptides, useful in
 PI diagnostics, forensics, gene mapping, identification of mutations
 PI responsible for genetic disorders or other traits and to assess
 PI biodiversity
 XX
 PS Claim 1: SEQ ID NO 24379; 103pp; English.
 XX
 CC The invention relates to isolated polynucleotide (I) and
 CC polypeptide (II) sequences. (I) is useful as hybridisation probes,
 CC polymerase chain reaction (PCR) primers, oligomers, and for chromosome
 CC and gene mapping, and in recombinant production of (II). The
 CC polynucleotides are also used in diagnostics as expressed sequence tags
 CC for identifying expressed genes. (I) is useful in gene therapy techniques
 CC to restore normal activity of (II) or to treat disease states involving
 CC (II). (II) is useful for generating antibodies against it, detecting or
 CC quantitating a polypeptide in tissue, as molecular weight markers and as
 CC a food supplement. (II) and its binding partners are useful in medical
 CC imaging of sites expressing (II). (I) and (II) are useful for treating
 CC disorders involving aberrant protein expression or biological activity.
 CC The polypeptide and polynucleotide sequences have applications in
 CC diagnostics, forensics, gene mapping, identification of mutations
 CC responsible for genetic disorders or other traits to assess biodiversity
 CC and to produce other types of data and products dependent on DNA and
 CC amino acid sequences. AAS64197-AAS94564 represent novel human
 CC diagnostic coding sequences of the invention.
 CC Note: the sequence data for this patent did not appear in the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 2370 BP; 579 A; 735 C; 599 G; 457 T; 0 other;

Query Match 84.0%; Score 16.8; DB 23; Length 2370;
 Best Local Similarity 90.0%; Pred. No. 68;
 Matches 18; Conservative 0; Mismatches 2; Indels 0; Gaps 0;
 QY 1 gctgatattctgggtggaaa 20
 DI 144 GCGGATATTCGTTGGGTAA 125
 RESULT 13
 AAS90850
 ID AAS90850 standard; CDNA; 2370 BP.
 AC AAS90850;
 XX
 DI 13-FEB-2002 (first entry)
 XX
 DE DNA encoding novel human diagnostic protein #26654.
 XX
 KW Human; chromosome mapping; gene mapping; gene therapy; forensic;
 KW food supplement; medical imaging; diagnostic; genetic disorder; ss.
 XX
 OS Homo sapiens.
 XX
 PN W0200175067-A2.
 XX
 PL 11-OCT-2001.
 XX
 PF 30-MAR-2001; 2001WO-US08631.
 XX
 PR 31-MAR-2000; 2000US-0540217.
 PR 23-AUG-2000; 2000US-0649167.
 XX
 PA (HYSE-) HYSEQ INC.
 XX
 PI Drmanac RT, Liu C, Tang YT;
 XX
 DR WPI: 2001-639362/73.

DR WPI: 2001-639362/73.
 DR P-PSDB: AAS26663.
 XX
 PI New isolated polynucleotide and encoded polypeptides, useful in
 PI diagnostics, forensics, gene mapping, identification of mutations
 PI responsible for genetic disorders or other traits and to assess
 PI biodiversity
 XX
 PS Claim 1: SEQ ID NO 26654; 103pp; English.
 XX
 CC The invention relates to isolated polynucleotide (I) and
 CC polypeptide (II) sequences. (I) is useful as hybridisation probes,
 CC polymerase chain reaction (PCR) primers, oligomers, and for chromosome
 CC and gene mapping, and in recombinant production of (II). The
 CC polynucleotides are also used in diagnostics as expressed sequence tags
 CC for identifying expressed genes. (I) is useful in gene therapy techniques
 CC to restore normal activity of (II) or to treat disease states involving
 CC (II). (II) is useful for generating antibodies against it, detecting or
 CC quantitating a polypeptide in tissue, as molecular weight markers and as
 CC a food supplement. (II) and its binding partners are useful in medical
 CC imaging of sites expressing (II). (I) and (II) are useful for treating
 CC disorders involving aberrant protein expression or biological activity.
 CC The polypeptide and polynucleotide sequences have applications in
 CC diagnostics, forensics, gene mapping, identification of mutations
 CC responsible for genetic disorders or other traits to assess biodiversity
 CC and to produce other types of data and products dependent on DNA and
 CC amino acid sequences. AAS64197-AAS94564 represent novel human
 CC diagnostic coding sequences of the invention.
 CC Note: the sequence data for this patent did not appear in the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 2370 BP; 457 A; 599 C; 735 G; 579 T; 0 other;

Query Match 84.0%; Score 16.8; DB 23; Length 2370;
 Best Local Similarity 90.0%; Pred. No. 68;
 Matches 18; Conservative 0; Mismatches 2; Indels 0; Gaps 0;
 QY 1 gctgatattctgggtggaaa 20
 Db 2227 gctgatattctgggtggaaa 2246
 RESULT 14
 AAS88821
 ID AAS88821 standard; CDNA; 2469 BP.
 AC AAS88821;
 XX
 DI 13-FEB-2002 (first entry)
 XX
 DE DNA encoding novel human diagnostic protein #24625.
 XX
 KW Human; chromosome mapping; gene mapping; gene therapy; forensic;
 KW food supplement; medical imaging; diagnostic; genetic disorder; ss.
 XX
 OS Homo sapiens.
 XX
 PN W0200175067-A2.
 XX
 PL 11-OCT-2001.
 XX
 PF 30-MAR-2001; 2001WO-US08631.
 XX
 PR 31-MAR-2000; 2000US-0540217.
 PR 23-AUG-2000; 2000US-0649167.
 XX
 PA (HYSE-) HYSEQ INC.
 XX
 PI Drmanac RT, Liu C, Tang YT;
 XX
 DR WPI: 2001-639362/73.

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OM nucleic - nucleic search, using sw model

Run on: July 18, 2002, 02:38:51 ; Search time 91.81 Seconds
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Title: US-09-632-657-7
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Sequence: 1 gctgatattctgtgggaaa 20

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Searched: 383533 seqs, 122816752 residues

Total number of hits satisfying chosen parameters: 767066

Minimum DB seq length: 0
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Listing first 45 summaries

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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	20	100.0	20	4	US-09-345-217-6
2	16.4	82.0	1848	1	US-08-313-553-10
3	16.4	82.0	1848	3	US-08-767-593-10
4	16.4	82.0	2246	4	US-09-032-742-3
5	16.4	82.0	2246	4	US-09-032-742-21
6	16.4	82.0	2246	4	US-09-032-742-22
7	16.4	82.0	2246	4	US-09-032-742-24
8	16.4	82.0	2246	4	US-09-032-742-25
9	15.8	79.0	3246	3	US-09-005-180A-2
10	15.2	76.0	711	4	US-08-998-416-900
11	15.2	76.0	10409	3	US-08-772-440-33
12	15.2	76.0	11933	4	US-09-470-618-13
13	15.2	76.0	11933	4	US-09-364-862-13
14	14.8	74.0	1313	1	US-08-461-731-3
15	14.8	74.0	1313	2	US-09-002-072B-3
16	14.8	74.0	1313	3	US-09-314-159-3
17	14.8	74.0	1313	5	PCT-US94-10465-1
18	14.8	74.0	1377	3	US-09-292-071-26
19	14.8	74.0	1377	3	US-09-292-071-28
20	14.8	74.0	1377	3	US-09-292-069A-26
21	14.8	74.0	1377	3	US-09-292-069A-28
22	14.8	74.0	1377	3	US-09-418-721-22
23	14.8	74.0	2733	1	US-08-310-271-1
24	14.8	74.0	2733	4	US-09-032-742-9
25	14.8	74.0	3011	1	US-07-821-715-1
26	14.4	72.0	1684	2	US-08-859-811-21
27	14.4	72.0	2428	3	US-08-475-742-15

ALIGNMENTS

RESULT 1

US-09-345-217-6
; Sequence 6, Application US/09345217
; Patent No. 6288442

GENERAL INFORMATION:

; APPLICANT: DUFF, GORDON W.
; APPLICANT: COX, ANGELA
; APPLICANT: CAMP, NICOLA J.
; APPLICANT: DIGIGVINE, FRANCESCO S.
; TITLE OF INVENTION: DIAGNOSTICS AND THERAPEUTICS FOR DISEASES ASSOCIATED
; TITLE OF INVENTION: WITH AN IL-1 INFLAMMATORY HAPLOTYPE
; FILE REFERENCE: NSA-010.02
; CURRENT APPLICATION NUMBER: US/09/345.217
; CURRENT FILING DATE: 1999-06-30
; EARLIER APPLICATION NUMBER: PCT/GB98/01481
; EARLIER FILING DATE: 1998-05-21
; EARLIER APPLICATION NUMBER: 9711040.7
; EARLIER FILING DATE: 1997-05-29
; NUMBER OF SEQ ID NOS: 32
; SOFTWARE: PatentIn Ver. 2.0

3

Query Match 100.0%; Score 20; DS 4; Length 20;
Best Local Similarity 100.0%; Pred. No. 0.093;
Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
Cg 1 gctgatattctgtgggaaa 20
|||||
Do 1 gctgatattctgtgggaaa 20

RESULT 2

US-08-313-553-10
; Sequence 10, Application US/08313553
; Patent No. 5641650

GENERAL INFORMATION:

; APPLICANT: TURNER, George J.
; APPLICANT: BETLACH, Mary C.
; TITLE OF INVENTION: EXPRESSION OF HETEROLOGOUS POLYPEPTIDES
; TITLE OF INVENTION: IN HALOBACTERIA
; NUMBER OF SEQUENCES: 15
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Walter H. Dreger

```
CLASSIFICATION: 435
ATTORNEY/AGENT INFORMATION:
NAME: Deger, Walter H.
REGISTRATION NUMBER: 24,190
REFERENCE/DOCKET NUMBER: A-57669/WHd
TELECOMMUNICATION INFORMATION:
TELEPHONE: (415) 781-1989
TELEFAX: (415) 398-3249
INFORMATION FOR SEQ ID NO: 10:
SEQUENCE CHARACTERISTICS:
LENGTH: 1848 base pairs
TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: cDNA
FEATURE:
NAME/KEY: misc_feature
LOCATION: 376..414
OTHER INFORMATION: /note= "Bacteriorhodopsin
OTHER INFORMATION: pre-sequence."
FEATURE:
NAME/KEY: terminator
LOCATION: 1756..1758
OTHER INFORMATION: /note= "Bacteriorhodopsin stop
OTHER INFORMATION: codon."
FEATURE:
NAME/KEY: misc_feature
LOCATION: 517..591
OTHER INFORMATION: /note= "Helix I of rat serotonin
OTHER INFORMATION: receptor protein (Type IC)."
FEATURE:
NAME/KEY: misc_feature
LOCATION: 625..690
OTHER INFORMATION: /note= "Helix II of rat serotonin
OTHER INFORMATION: receptor protein (Type IC)."
FEATURE:
NAME/KEY: misc_feature
LOCATION: 736..807
OTHER INFORMATION: /note= "Helix III of rat serotonin
OTHER INFORMATION: receptor protein (Type IC)."
FEATURE:
NAME/KEY: misc_feature
LOCATION: 868..939
OTHER INFORMATION: /note= "Helix IV of rat serotonin
OTHER INFORMATION: receptor protein (Type IC)."
FEATURE:
NAME/KEY: misc_feature
LOCATION: 997..1059
OTHER INFORMATION: /note= "Helix V of rat serotonin
OTHER INFORMATION: receptor protein (Type IC)."
FEATURE:
NAME/KEY: misc_feature
LOCATION: 1297..1362
OTHER INFORMATION: /note= "Helix VI of rat serotonin
OTHER INFORMATION: receptor protein (Type IC)."
FEATURE:
NAME/KEY: misc_feature
LOCATION: 1411..1476
OTHER INFORMATION: /note= "Helix VII of rat serotonin
OTHER INFORMATION: receptor protein (Type IC)."
FEATURE:
NAME/KEY: mutation
LOCATION: replace(213, "")
OTHER INFORMATION: /note= "G to A mutation removes
OTHER INFORMATION: AlwNI restriction site."
FEATURE:
NAME/KEY: misc_feature
LOCATION: 1732..1734
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OTHER INFORMATION: C-terminal amino acid of the rat serotonin
OTHER INFORMATION: receptor protein (Type IC)."
NAME/KEY: misc_signal
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LOCATION: 374
OTHER INFORMATION: /note= "RNA start site."
FEATURE:
NAME/KEY: CDS
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OTHER INFORMATION: /note= "Serotonin stop codon."
FEATURE:
NAME/KEY: repeat_region
LOCATION: 436..462
OTHER INFORMATION: /note= "Sequence encoding
Patent No. 6010885
OTHER INFORMATION: polypartitic acid."
FEATURE:
NAME/KEY: mutation
LOCATION: replace(1755, "")
OTHER INFORMATION: /note= "C to T mutation removes
OTHER INFORMATION: AlwNI restriction site."
US-08-767-993-10
Query Match 82.0%; Score 16.4; DB 3; Length 1848;
Best Local Similarity 94.4%; Pred. No. 13;
Matches 17; Conservative 0; Mismatches 1; Indels 0; Gaps 0;
QY 1 gcgatattcttggtggga 18
|||||
CD 645 GCAGATATCTGTTGGGA 666
|||||
RESULT 4
US-09-032-742-3
Sequence 3: Application US/09032742
Patent No. 6255089
GENERAL INFORMATION:
APPLICANT: Teitler, Milt
APPLICANT: Herrick-Davis, Katharine
APPLICANT: Egan, Christina C.
TITLE OF INVENTION: Constitutively Activated Serotonin
NUMBER OF SEQUENCES: 25
CORRESPONDENCE ADDRESS:
ADDRESSEE: Laurence Weinberger
STREET: 882 S. Matlack Street, Suite 103
STREET: P.O. Box 1663
CITY: West Chester
STATE: PA
COUNTRY: USA
ZIP: 19380-0053
COMPUTER READABLE FORM:
MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC Compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: PatentIn Release #1.0, Version #1.30
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/032.742
FILING DATE: 27-FEB-1998
CLASSIFICATION: 536
ATTORNEY/AGENT INFORMATION:
NAME: Weinberger, Laurence
REGISTRATION NUMBER: 27,965
REFERENCE/DOCKET NUMBER: 3086-4
TELECOMMUNICATION INFORMATION:
TELEPHONE: (610) 431-1703
TELEFAX: (610) 431-4181
INFORMATION FOR SEQ ID NO: 3:
SEQUENCE CHARACTERISTICS:
LENGTH: 2246 base pairs
TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
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APPLICATION NUMBER: US/09/032,742
FILING DATE: 27-FEB-1998
CLASSIFICATION: 536
ATTORNEY/AGENT INFORMATION:
NAME: Weinberger, Laurence
REGISTRATION NUMBER: 27,965
REFERENCE/DOCKET NUMBER: 3086-4
TELECOMMUNICATION INFORMATION:
TELEPHONE: (610) 431-1703
TELEFAX: (610) 431-4181
INFORMATION FOR SEQ ID NO: 24:
SEQUENCE CHARACTERISTICS:
LENGTH: 2246 base pairs
TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: DNA (genomic)
US-09-032-742-24

Query Match 82.0%; Score 16.4; DB 4; Length 2246;
Best Local Similarity 94.4%; Pred. No. 13;
Matches 17; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 gctgatatctgtggtgga 18
||||| |||||||
DB 982 GCATGATGCTGGTGGGA 999

RESULT 8
US-09-032-742-25
Sequence 25, Application US/09032742
Patent No. 6255089
GENERAL INFORMATION:
APPLICANT: Tetlier, Milt
APPLICANT: Herrick-Davis, Katharine
APPLICANT: Egan, Christina C.
TITLE OF INVENTION: Constitutively Activated Serotonin
NUMBER OF SEQUENCES: 25
CORRESPONDENCE ADDRESS:
ADDRESSEE: Laurence Weinberger
STREET: 882 S. Matlack Street, Suite 103
CITY: West Chester
STATE: PA
COUNTRY: USA
ZIP: 19380-0053
COMPUTER READABLE FORM:
MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: PatentIn Release #1.0, Version #1.30
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/032,742
FILING DATE: 27-FEB-1998
CLASSIFICATION: 536
ATTORNEY/AGENT INFORMATION:
NAME: Weinberger, Laurence
REGISTRATION NUMBER: 27,965
REFERENCE/DOCKET NUMBER: 3086-4
TELECOMMUNICATION INFORMATION:
TELEPHONE: (610) 431-1703
TELEFAX: (610) 431-4181
INFORMATION FOR SEQ ID NO: 25:
SEQUENCE CHARACTERISTICS:
LENGTH: 2246 base pairs
TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: DNA (genomic)
US-09-032-742-25

Query Match 82.0%; Score 16.4; DB 4; Length 2246;
Best Local Similarity 94.4%; Pred. No. 13;
Matches 17; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 gctgatatctgtggtgga 18
||||| |||||||
DB 982 GCATGATGCTGGTGGGA 999

RESULT 9
US-09-005-180A-2/C
Sequence 2, Application US/09005180A
Patent No. 612446
GENERAL INFORMATION:
APPLICANT: Hillman, Jennifer L.
APPLICANT: Corley, Neil C.
APPLICANT: Shah, Purvi
TITLE OF INVENTION: HUMAN VPS35/MEM3-RELATED PROTEIN
NUMBER OF SEQUENCES: 4
CORRESPONDENCE ADDRESS:
ADDRESSEE: Incyte Pharmaceuticals, Inc.
STREET: 3174 Porter Dr.
CITY: Palo Alto
STATE: CA
COUNTRY: USA
ZIP: 94304
COMPUTER READABLE FORM:
MEDIUM TYPE: Diskette
COMPUTER: IBM Compatible
OPERATING SYSTEM: DOS
SOFTWARE: FastSeq for Windows Version 2.0
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/005,180A
FILING DATE: Filed January 8, 1998
CLASSIFICATION: 424
PRIOR APPLICATION DATA:
APPLICATION NUMBER:
FILING DATE:
ATTORNEY/AGENT INFORMATION:
NAME: Billings, Lucy J.
REGISTRATION NUMBER: 36,749
REFERENCE/DOCKET NUMBER: Pf-0457 US
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650-855-0555
TELEFAX: 650-845-4166
TELEX:
INFORMATION FOR SEQ ID NO: 2:
SEQUENCE CHARACTERISTICS:
LENGTH: 3246 base pairs
TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
IMMEDIATE SOURCE:
LIBRARY: LUNGTUT08
CLONE: 2641812
US-09-005-180A-2

Query Match 79.0%; Score 15.8; DB 3; Length 3246;
Best Local Similarity 89.5%; Pred. No. 26;
Matches 17; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

QY 2 ctgatatctgtggtgga 20
||||| |||||||
DB 1785 CTGATGCTGGTGGCAA 1767

RESULT 10
US-08-998-416-900
Sequence 900, Application US/08998416
Patent No. 6239264
GENERAL INFORMATION:

Db 2010 GCTGATATTATAGTGGGAA 2029

RESULT 12

US-09-470-618-13/c
; Sequence 13, Application US/09470618
; Patent No. 6200560
; GENERAL INFORMATION:
; APPLICANT: Couto, Linda B.
; APPLICANT: Colosi, Peter C.
; TITLE OF INVENTION: Adeno-Associated Vectors for Expression of Factor VIII
; FILE REFERENCE: Avigen-04082
; CURRENT APPLICATION NUMBER: US/09/470,618
; CURRENT FILING DATE: 1999-12-22
; EARLIER APPLICATION NUMBER: 09/364,862
; EARLIER FILING DATE: 1999-07-30
; EARLIER APPLICATION NUMBER: 60/125,974
; EARLIER FILING DATE: 1999-03-24
; EARLIER APPLICATION NUMBER: 60/104,994
; EARLIER FILING DATE: 1998-10-20
; NUMBER OF SEQ ID NOS: 15
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 13
; LENGTH: 11933
; TYPE: DNA
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Synthetic
US-09-470-618-13

Query Match 76.0%; Score 15.2; DB 4; Length 11933;

Best Local Similarity 85.0%; Pred. No. 70; Mismatches 0; Indels 0; Gaps 0;
Matches 17; Conservative 0

QY 1 gctgatattctgtgggaaa 20
||||| ||||||| |||||||
Db 8451 GCTGCATTCTGGAGGAAA 8432

RESULT 13

US-09-364-862-13/c
; Sequence 13, Application US/09364862
; Patent No. 6221349
; GENERAL INFORMATION:
; APPLICANT: Couto, Linda B.
; APPLICANT: Colosi, Peter C.
; TITLE OF INVENTION: ADENO-ASSOCIATED VECTORS FOR EXPRESSION OF FACTOR VIII
; TITLE OF INVENTION: BY TARGET
; FILE REFERENCE: AVIGEN-03743
; CURRENT APPLICATION NUMBER: US/09/364,862
; CURRENT FILING DATE: 1999-07-30
; EARLIER APPLICATION NUMBER: 60/125,974
; EARLIER FILING DATE: 1999-03-24
; EARLIER APPLICATION NUMBER: 60/104,994
; EARLIER FILING DATE: 1998-10-20
; NUMBER OF SEQ ID NOS: 14
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 13
; LENGTH: 11933
; TYPE: DNA
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-364-862-13

Query Match 76.0%; Score 15.2; DB 4; Length 11933;

Best Local Similarity 85.0%; Pred. No. 70; Mismatches 0; Indels 0; Gaps 0;
Matches 17; Conservative 0

QY 1 gctgatattctgtgggaaa 20
||||| ||||||| |||||||
Db 8451 GCTGCATTCTGGAGGAAA 8432

RESULT 14

US-08-461-731-3/c
; Sequence 3, Application US/08461731
; Patent No. 5716806
; GENERAL INFORMATION:
; APPLICANT: MEISSNER, ET AL.
; TITLE OF INVENTION: Human Inositol Monophosphatase H1
; NUMBER OF SEQUENCES: 9
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: CARELLA, BYRNE, BAIN, GILFILLAN,
; ADDRESSEE: CECCHI, STEWART & OLSTEIN
; STREET: 6 BECKER FARM ROAD
; CITY: ROSELAND
; STATE: NEW JERSEY
; COUNTRY: USA
; ZIP: 07068
; COMPUTER READABLE FORM:
; MEDIUM TYPE: 3.5 INCH DISKETTE
; COMPUTER: IBM PS/2
; OPERATING SYSTEM: MS-DOS
; SOFTWARE: WORD PERFECT 5.1
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/461,731
; FILING DATE: June 5, 1995
; CLASSIFICATION: 435
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: PCT/US94/10465
; FILING DATE: 16 SEP 94
; ATTORNEY/AGENT INFORMATION:
; NAME: FERRARO, GREGORY D.
; REGISTRATION NUMBER: 36,134
; REFERENCE/DOCKET NUMBER: 325800-316
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 201-994-1700
; TELEFAX: 201-994-1744
; INFORMATION FOR SEQ ID NO: 3:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 1313 BASE PAIRS
; TYPE: NUCLEIC ACID
; STRANDEDNESS: SINGLE
; TOPOLOGY: LINEAR
; MOLECULE TYPE: CDNA
US-08-461-731-3

Query Match 74.0%; Score 14.8; DB 1; Length 1313;
Best Local Similarity 88.9%; Pred. No. 80;
Matches 16; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

QY 3 tgatattctgtgggaaa 20
||||| ||||||| |||||||
Db 1202 TTATATTCGGGGGAAA 1185

RESULT 15

US-09-002-072a-3/c
; Sequence 3, Application US/09002072B
; Patent No. 5955339
; GENERAL INFORMATION:
; APPLICANT: Meissner, Paul et al.
; TITLE OF INVENTION: Human Inositol Monophosphatase H1
; NUMBER OF SEQUENCES: 10
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Human Genome Sciences, Inc.
; STREET: 9410 Key West Avenue
; CITY: Rockville
; STATE: MD
; COUNTRY: USA

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Copyright (C) 1993 - 2000, CompuGen Ltd.

OM nucleic - nucleic search, using sw model

Run On: July 18, 2002, 02:34:06 ; Search time 2539.01 seconds

(without alignments)
106.317 million cell updates/sec

Title: US-09-632-657-7

Perfect score: 20

Sequence: 1 gctgatattctggtggaaa 20

Scoring table: IDENTITY_NUC
Gapop 10.0, Gapext 1.0

Searched: 13736207 seqs, 6748477542 residues

Total number of hits satisfying chosen parameters: 27472414

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database :

EST:**

1: em_esth:.*
2: em_esth:.*
3: em_esth:.*
4: em_esth:.*
5: em_esth:.*
6: em_esth:.*
7: em_esth:.*
8: em_esth:.*
9: gb_est1:.*
10: gb_est2:.*
11: gb_hic:.*
12: gb_gss:.*
13: em_gss_hum:.*
14: em_gss_inv:.*
15: em_gss_pln:.*
16: em_gss_vrt:.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
C 1	18	90.0	533	12	AQ410722 HS_5067_A
C 2	18	90.0	551	10	BM188182
C 3	18	90.0	729	10	BE913740
C 4	17.4	87.0	617	12	AZ458703
C 5	17.4	87.0	651	10	BI066862
C 6	17.4	87.0	688	12	AG181383
C 7	17.4	87.0	697	12	AG181375
C 8	17	85.0	176	9	AV011849
C 9	17	85.0	195	9	AV293951
C 10	17	85.0	219	9	BB067695
C 11	17	85.0	248	9	BB047357
C 12	17	85.0	452	12	AQ819189
C 13	17	85.0	519	12	AQ437759
C 14	16.8	84.0	132	12	AQ420981
C 15	16.8	84.0	154	10	BF758769
C 16	16.8	84.0	218	9	AV333398
C 17	16.8	84.0	248	10	BF950269

C 18	16.8	84.0	555	12	AQ267714
C 19	16.8	84.0	376	10	BF950329
C 20	16.8	84.0	387	9	AI771884
C 21	16.8	84.0	335	9	AW521782
C 22	16.8	84.0	345	10	BF186914
C 23	16.8	84.0	403	9	AW801704
C 24	16.8	84.0	405	9	AI490092
C 25	16.8	84.0	405	9	AI897010
C 26	16.8	84.0	407	12	AQ014285
C 27	16.8	84.0	422	10	N21831
C 28	16.8	84.0	427	10	BF188475
C 29	16.8	84.0	437	10	BF187039
C 30	16.8	84.0	451	9	AI484102
C 31	16.8	84.0	459	12	TA1H020
C 32	16.8	84.0	484	10	BF187458
C 33	16.8	84.0	500	12	AQ420978
C 34	16.8	84.0	556	12	AQ189596
C 35	16.8	84.0	570	12	AQ827212
C 36	16.8	84.0	577	12	AZ695965
C 37	16.8	84.0	612	12	AZ274985
C 38	16.8	84.0	621	10	BG350691
C 39	16.8	84.0	707	12	AQ162826
C 40	16.8	84.0	718	10	BG598861
C 41	16.8	84.0	764	10	BG889296
C 42	16.8	84.0	770	10	BI405464
C 43	16.8	84.0	891	10	BF262465
C 44	16.8	84.0	1021	12	CN506PKX
C 45	16.8	84.0	1642	10	BI489140

ALIGNMENTS

RESULT 1
AQ410722/c
LOCUS HS_5067_A1_C03_17A RPOI-11 Human Male BAC Library Homo sapiens
DEFINITION genomic clone Plate-643 Col-5 Row-E, DNA sequence.
ACCESSION AQ410722
VERSION AQ410722.1 GI:4127915
KEYWORDS GSS.
SOURCE Human.
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
REFERENCE 1 (bases 1 to 533)
Kellier, A., Shaker, R., Furlong, J., Young, J., Zhao, S., Adams, M.D., and Hoot, L.
IIIIE
Sequence-tagged connectors: A sequence approach to mapping and scanning the human genome
Proc. Natl. Acad. Sci. U. S. A. 96 (17), 9739-9744 (1999)
95390589
COMMENT
Contact: Mahairas GG, Wallace JC, Hood L
High Throughput Sequencing Center
University of Washington
401 Queen Anne Avenue North, Seattle, WA 98109, USA
Tel: (206) 616-3618
Fax: (206) 616-3887
Email: jwallace@u.washington.edu
Clones are derived from the human BAC library RPOI-11. For BAC library availability, please contact Pieter de Jong (pieter@dejong.med.buffalo.edu). Clones may be purchased from BACPAC Resources (http://bacpac.med.buffalo.edu/ordering_bac.htm) or from Research Genetics (info@resgen.com). BAC end Web Server: http://www.htsc.washington.edu
Plasmid: 643 row: E column: 5
Seq primer: 17
Class: BAC ends
High quality sequence stop: 533.
Location/Qualifiers
1..533
/organism="Homo sapiens"

ORIGIN

Query Match 90.0%; Score 18; DB 10; Length 725;
Best Local Similarity 100.0%; Pred. No. 2.5e+02;
Matches 18; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 2 ctgatattctgtggaaa 19
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DB 703 CTGATATCTCGTGGGAAA 720

RESULT 4

A2458703/c
LOCUS A2458703 617 bp DNA linear GSS 01-CCR-2000
DEFINITION IM0263105F Mouse 10kb plasmid UUGCLM library Mus musculus genomic
clone UUGCLM0263105 F, DNA sequence.

ACCESSION A2458703
VERSION A2458703.1 GI:10616828
KEYWORDS GSS.
SOURCE house mouse.

ORGANISM Mus musculus
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
1 (bases 1 to 617)

AUTHORS Dunn, D., Aoyagi, A., Barber, M., Beacorn, T., Duval, B., Hamil, C.,
Islam, H., Longacre, S., Mahmoud, M., Meenen, E., Pedersen, T., Reilly,
M., Rose, M., Rose, R., Stokes, R., Tingey, A., von Niederhausern, A.
and Wright, D., Weiss, R.

TITLE Mouse whole genome scaffolding with paired end reads from 10kb
plasmid inserts

JOURNAL Unpublished (2000)
COMMENT Contact: Robert B. Weiss
University of Utah Genome Center
Rm. 308, Biomedical Polymers Research Bldg., 20 S. 2030 E., SLC, UT
84112, USA
Tel: 801 585 5606
Fax: 801 585 7177
Email: ddunn@genetics.utah.edu

Insert Length: 10000 Std Error: 0.00
Plate: 0263 row: 1 column: 05
Seq primer: CGTTGTAACGACGGCCAGT
Class: plasmid ends

High quality sequence stop: 617.
Location/Qualifiers

FEATURES
source

1..617
/organism="Mus musculus"
/strain="C57BL/6J"
/db_xref="taxon:10090"
/clone="UUGCLM0263105"
/clone_lib="Mouse 10kb plasmid UUGCLM library"
/sex="Male"
/lab_host="E. Coli strain XL10-Gold, Tl-resistant, F"
/note="Vector: pWD42nv; Purified genomic DNA from M.
musculus C57BL/6J (male) was obtained from the Jackson
Laboratory Mouse DNA Resource
(http://www.jax.org/resources/documents/dnares/). The DNA
was hydrodynamically sheared by repeated passage through a
0.005 inch orifice at constant velocity. The sheared DNA
was blunt end-repaired with T4 DNA polymerase and 14
polynucleotide kinase. Adaptor oligonucleotides were
ligated to the blunt ends in high molar excess. The
adapted DNA was purified and size-selected for a 5.5 to
10.5 kb range using preparative agarose gel
electrophoresis. Vector DNA was prepared from a derivative
of pWD42 (G114732114/gb/AF129072.1), a copy-number
inducible derivative of plasmid R1. The vector was ligated
with adaptors complementary to the insert adaptors and
purified. The sheared, adapted mouse DNA was annealed to
adapted vector DNA, and transformed into
chemically-competent E. coli XL10-Gold (Stratagene) cells
and selected for ampicillin resistance."

BASE COUNT 155 a 173 c 118 g 171 t
ORIGIN

Query Match 87.0%; Score 17.4; DB 12; Length 617;
Best Local Similarity 94.7%; Pred. No. 4.7e+02;
Matches 18; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 2 ctgatattctgtggaaa 20
||||| ||||||| |||||||
DB 336 CCGAATCTCGTGGGAAA 378

RESULT 5

B1065862/c
LOCUS B1065862 651 bp mRNA linear EST 15-JUN-2001
DEFINITION p31n.pk009.120 normalized chicken fat cDNA library Gallus gallus
cDNA clone p31n.pk009.120 5' similar to p31n.JC4256/JC4256
hypothetical 32.0k protein - Neurospora crassa gb|AAC41672.1|
(L40806) open reading frame (Neurospora crassa) p31n.JC4256/JC4256 ORF
[Neurospora crassa]g, mRNA sequence.

ACCESSION B1065862
VERSION B1065862.1 GI:14474384
KEYWORDS EST.
SOURCE chicken.

ORGANISM Gallus gallus
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Archosauria; Aves; Neognathae; Galliformes; Phasianidae;
Phasianinae; Gallus.

REFERENCE 1 (bases 1 to 651)
AUTHORS Cogburn, L.A., Morgan, R.W. and Burnside, J.
TITLE Chicken ESTs from fat
JOURNAL Unpublished (2001)
COMMENT Contact: Larry A. Cogburn
University of Delaware
Townsend Hall, Newark, DE 19717, USA
Tel: 302-831-1335
Fax: 302-831-2822
Email: cogburn@udel.edu, www.chickest.udel.edu.

FEATURES
source

1..651
/organism="Gallus gallus"
/db_xref="taxon:9031"
/clone="p31n.pk009.120"
/clone_lib="normalized chicken fat cDNA library"
/sex="Male and Female"
/tissue_type="fat"
/lab_host="E.coli EMDH108"
/note="Vector: pSPOR11"

BASE COUNT 174 a 141 c 166 g 158 t 12 others

Query Match 87.0%; Score 17.4; DB 10; Length 651;
Best Local Similarity 94.7%; Pred. No. 4.8e+02;
Matches 18; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 gcgatattctgtggaaa 19
||||| ||||||| |||||||
DB 551 CCGAATCTCGTGGGAAA 533

RESULT 6

AG181383
LOCUS AG181383 688 bp DNA linear GSS 09-JAN-2002
DEFINITION Pan troglodytes DNA, clone: RP43-054D23.T7, genomic survey
sequence.
ACCESSION AG181383
VERSION AG181383.1 GI:16711063
KEYWORDS GSS; GSS (genome survey sequence).
SOURCE Pan troglodytes male lymphocytes DNA, clone: RP43-054D23.T7.
Male BAC Library clone: RP43-054D23.T7.
ORGANISM Pan troglodytes

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/clone_lib="Mus musculus 18-day embryo C57BL/6J"
/sex="mixed"
/dev_stage="18-day embryo"
/lab_host="41 C 43 g 52 t"

BASE COUNT 40 a 41 c 43 g 52 t
ORIGIN

Query Match 85.0%; Score 17; DB 9; Length 176;
Best local Similarity 100.0%; Pred. No. 5.9e+02;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 2 ctgattatctggtgga 18
DB 36 ctgattatctggtgga 52

RESULT 9
LOCUS AV293951 195 bp mRNA linear EST 10-NOV-1999
DEFINITION AV293951 RIKEN full-length enriched, 10 days neonate head Mus
musculus cDNA clone 5330401C20 3', mRNA sequence.
VERSION AV293951
KEYWORDS EST
SOURCE house mouse.
ORGANISM Mus musculus.
REFERENCE Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
1 (bases 1 to 195)
AUTHORS Konno,H., Aizawa,K., Akahira,S., Akiyama,J., Carninci,P., Endo,T.,
Fukuda,S., Fukunishi,Y., Hara,A., Hayatsu,N., Hirozane,I., Horii,F.,
Ishii,Y., Ishikawa,T., Itoh,M., Izawa,M., Kadota,K., Kagawa,I., Kai
,C., Kawai,J., Kikuchi,N., Kojima,Y., Koya,S., Kusakabe,M.,
Matsuyama,T., Miki,R., Mizuno,Y., Nakamura,M., Oda,H., Okazaki,Y.,
Owa,C., Ozawa,Y., Saito,H., Sano,M., Sato,K., Shibata,K., Shibata
,Y., Shigemoto,Y., Shiraki,T., Sogabe,Y., Sugahara,Y., Suzuki,H.,
Suzuki,H., Takahashi,F., Tateo,M., Tominaga,N., Tsunoda,Y.,
Watahiki,A., Watanabe,S., Yamamura,T., Yasunishi,A., Yokota,T.,
Yoshiki,A., Yoshino,M., Muramatsu,M. and Hayashizaki,Y.
RIKEN Mouse ESTs (Konno,H., et al. 1999)
Unpublished (1999)
Contact: Yoshihide Hayashizaki
Laboratory for Genome Exploration Research Group, RIKEN Genomic
Sciences Center(GSC), Yokohama Institute
The Institute of Physical and Chemical Research (RIKEN)
1-7-22 Suehiro-cho, Tsurumi-ku, Yokohama, Kanagawa 230-0045, Japan
Tel: 81-45-503-9222
Fax: 81-45-503-9216
Email: genome-res@sc.riken.go.jp.
URL: http://genome.gsc.riken.go.jp/
Sasaki,N., Izawa,M., Watahiki,M., Ozawa,K., Tanaka,T., Yoneda,Y.,
Matsura,S., Carninci,P., Muramatsu,M., Okazaki,Y. and Hayashizaki
,Y.
Transcriptional sequencing: A method for DNA sequencing using RNA
polymerase. Proc. Natl. Acad. Sci. U.S.A. 95 (7), 3455-3460 (1998)
Itoh,M., Kitsuai,T., Akiyama,J., Shibata,K., Izawa,M., Kawai,J.
Tomaru,Y., Carninci,P., Shibata,Y., Ozawa,Y., Muramatsu,M., Okazaki
,Y. and Hayashizaki,Y.
Automated filtration-based high-throughput plasmid preparation
system. Genome Res. 9 (5), 463-470 (1999)
Carninci,P. and Hayashizaki,Y.
High-efficiency full-length cDNA cloning. Methods Enzymol. 303,
19-44 (1999)
Please visit our web site (http://genome.rtc.riken.go.jp) for
further details.
FEATURES
source Location/Qualifiers
1..195
/organism="Mus musculus"
/strain="C57BL/6J"
/db_xref="taxon:10090"
/clone="5330401C20"
/clone_lib="RIKEN full-length enriched, 10 days neonate
head"

```

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/sex="mixed"
/tissue_type="head"
/dev_stage="10 days neonate"
/lab_host="DB105"
/notes="Site 1: Sall; Site 2: BamHI; cDNA library was
prepared and sequenced in Mouse Genome Encyclopedia
Project of Genome Exploration Research Group in Riken.
Genomic Sciences Center and Genome Science Laboratory in
RIKEN, Division of Experimental Animal Research in Riken.
Contributed to prepare mouse tissues. 1st strand cDNA was
primed with a primer [5'
GAGAGAGAGAGATCCAGAGCTCTTTTIIIIIIIVN 3'], cDNA was
prepared by using trehalose thermo-activated reverse
transcriptase and subsequently enriched for full-length by
cap-trapper. cDNA went through one round of normalization
to Rot = 10.0 and subtraction to Rot = 100.0. Second
strand cDNA was prepared with the primer adapter of
sequence [5' GAGAGAGATCTGAGTAAATAAATAATACCCCCC00000
3']. cDNA was cloned into the XhoI and BamHI sites.
Vector: a modified pBluescript KS(+) after bulk excision
from lambda FLC I. Cloning sites, 5' end: Sall; 3' end:
BamHI."
BASE COUNT 40 a 43 c 39 g 73 t
ORIGIN

Query Match 85.0%; Score 17; DB 9; Length 195;
Best local Similarity 100.0%; Pred. No. 6e+02;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 2 ctgattatctggtgga 18
DB 57 ctgattatctggtgga 73

RESULT 10
LOCUS BB067695 219 bp mRNA linear EST 25-JUN-2000
DEFINITION BB067695 RIKEN full-length enriched, 15 days embryo male testis Mus
musculus cDNA clone 803046B06 3', mRNA sequence.
VERSION BB067695
KEYWORDS EST.
SOURCE house mouse.
ORGANISM Mus musculus.
REFERENCE Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
1 (bases 1 to 219)
AUTHORS Konno,H., Aizawa,K., Akahira,S., Akiyama,J., Arakawa,T., Carninci
,P., Endo,T., Fukuda,S., Fukunishi,Y., Hara,A., Hayatsu,N.,
Hirozane,I., Horii,F., Ishii,Y., Ishikawa,J., Ishikawa,T., Itoh,M.
Izawa,M., Kadota,K., Kagawa,I., Kai,C., Kawai,J., Kikuchi,N.,
Kiyosawa,H., Kojima,Y., Kondo,S., Koya,S., Kurihara,C., Kusakabe,M.
Matsuyama,T., Miki,R., Mizuno,Y., Nakamura,M., Oda,H., Okazaki,Y.
Owa,C., Saito,H., Sakai,C., Sato,K., Shibata,K., Shibata
,Y., Shigemoto,Y., Shinagawa,A., Shiraki,T., Sogabe,Y., Sugahara
,Y., Suzuki,H., Suzuki,H., Tagawa,A., Takahashi,F., Tominaga,N., Toya
,I., Tsunoda,Y., Watahiki,A., Watanabe,S., Yamamura,T., Yamakaki
,Y., Yasunishi,A., Yokota,T., Yoshida,K., Yoshiki,A., Yoshino
,M., Muramatsu,M. and Hayashizaki,Y.
RIKEN Mouse ESTs (Konno,H., et al.)
Unpublished (2000)
Contact: Yoshihide Hayashizaki
Laboratory for Genome Exploration Research Group, RIKEN Genomic
Sciences Center(GSC), Yokohama Institute
The Institute of Physical and Chemical Research (RIKEN)
1-7-22 Suehiro-cho, Tsurumi-ku, Yokohama, Kanagawa 230-0045, Japan
Tel: 81-45-503-9222
Fax: 81-45-503-9216
Email: genome-res@sc.riken.go.jp.
URL: http://genome.gsc.riken.go.jp/
Carninci,P., Nishiyama,Y., Westover,A., Itoh,M., Nagaoka,S., Sasaki
,N., Okazaki,Y., Muramatsu,M. and Hayashizaki,Y.

```

16 34 CTGATATCTGTGGGA 50

RESULT 12
A0819189/c

LOCUS HS_5300_A2_E07_SP6E_RPCI-11 Human Male BAC Library Homo sapiens
DEFINITION genomic clone Plate-876 Col=14 Row=1, DNA sequence.

ACCESSION A0819189
VERSION A0819189.1 GI:5781582
KEYWORDS GSS.

SOURCE
ORGANISM

Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
1 (bases 1 to 452)
Mahairas, G.G., Wallace, J.C., Smith, K., Swartzell, S., Holzman, I.,
Keller, A., Shaker, R., Furlong, J., Young, J., Zhao, S., Adams, M.D. and
Hood, L.

TITLE
Sequence-tagged connectors: A sequence approach to mapping and
scanning the human genome

JOURNAL
MEDLINE
COMMENT

Contact: Mahairas GG, Wallace JC, Hood L
High Throughput Sequencing Center
University of Washington
401 Queen Anne Avenue North, Seattle, WA 98109, USA
Tel: (206) 616-3618
Fax: (206) 616-3887

Email: jwallaceu.washington.edu
Clones are derived from the human BAC library RPCI-11. For BAC
library availability, please contact Pieter de Jong
(pieterdejong.med.buffalo.edu). Clones may be purchased from
BACPAC Resources (http://bacpac.med.buffalo.edu/ordering_bac.htm)
or from Research Genetics (info@resgen.com). BAC end Web Server:
http://www.htsc.washington.edu
Plate: 876 row: 1 column: 14
Seq primer: SP6
Class: BAC ends
High quality sequence stop: 452.

FEATURES
source

Location/Qualifiers
1..452
/organism="Homo sapiens"
/db_xref="taxon:9606"
/clone="Plate-876 Col=14 Row=1"
/clone_lib="RPCI-11 Human Male BAC Library"
/sex="male"
/note="Vector: pPACE3.6; Site_1: EcoRI; Site_2: EcoRI;
Male blood DNA was isolated from one randomly chosen donor
and partially digested with a combination of EcoRI and
EcoRI Methylase. Size selected DNA was cloned into the
pPACE3.6 vector at EcoRI sites"
BASE COUNT 147 a 66 c 89 g 148 t 2 others
ORIGIN

Query Match 85.0%; Score 17; DB 12; Length 452;
Best Local Similarity 100.0%; Pred. No. 6.9e-02;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 4 gatattctgtgggaaa 20
|||||
DB 366 GATATCTGTGGGAAA 350

RESULT 13
A0437759/c

LOCUS HS_5056_B1_F03_T7A_RPCI-11 Human Male BAC Library Homo sapiens
DEFINITION genomic clone Plate-632 Col=5 Row=L, DNA sequence.

ACCESSION A0437759
VERSION A0437759.1 GI:4549098
KEYWORDS GSS.

SOURCE
ORGANISM

Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
1 (bases 1 to 519)
Mahairas, G.G., Wallace, J.C., Smith, K., Swartzell, S., Holzman, I.,
Keller, A., Shaker, R., Furlong, J., Young, J., Zhao, S., Adams, M.D. and
Hood, L.

TITLE
Sequence-tagged connectors: A sequence approach to mapping and
scanning the human genome

JOURNAL
MEDLINE
COMMENT

Contact: Mahairas GG, Wallace JC, Hood L
High Throughput Sequencing Center
University of Washington
401 Queen Anne Avenue North, Seattle, WA 98109, USA
Tel: (206) 616-3618
Fax: (206) 616-3887

Email: jwallaceu.washington.edu
Clones are derived from the human BAC library RPCI-11. For BAC
library availability, please contact Pieter de Jong
(pieterdejong.med.buffalo.edu). Clones may be purchased from
BACPAC Resources (http://bacpac.med.buffalo.edu/ordering_bac.htm)
or from Research Genetics (info@resgen.com). BAC end Web Server:
http://www.htsc.washington.edu
Plate: 632 row: 1 column: 5

Seq primer: 17
Class: BAC ends
High quality sequence stop: 519.

FEATURES
source

Location/Qualifiers
1..519
/organism="Homo sapiens"
/db_xref="taxon:9606"
/clone="Plate-632 Col=5 Row=L"
/clone_lib="RPCI-11 Human Male BAC Library"
/sex="male"
/note="Vector: pPACE3.6; Site_1: EcoRI; Site_2: EcoRI;
Male blood DNA was isolated from one randomly chosen donor
and partially digested with a combination of EcoRI and
EcoRI Methylase. Size selected DNA was cloned into the
pPACE3.6 vector at EcoRI sites"
BASE COUNT 161 a 85 c 103 g 165 t 5 others
ORIGIN

Query Match 85.0%; Score 17; DB 12; Length 519;
Best Local Similarity 100.0%; Pred. No. 7.1e-02;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 4 gatattctgtgggaaa 20
|||||
DB 382 GATATCTGTGGGAAA 366

RESULT 14
A0420581

LOCUS RPCI-11-210121.TV RPCI-11 Homo sapiens genomic clone RPCI-11-210121
DEFINITION DNA sequence.

ACCESSION A0420581
VERSION A0420581.1 GI:4478705
KEYWORDS GSS.

SOURCE
ORGANISM

Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
1 (bases 1 to 132)
Zhao, S., Adams, M.D., Nierman, W., Malek, J., de Jong, P. and Venter
J.C.

TITLE
Map Building
Use of BAC End Sequences from Library RPCI-11 for Sequence-Ready
Map Building

JOURNAL
COMMENT
Unpublished (1997)
Contact: Shaying Zhao, William Nierman, Mark Adams

Department of Eukaryotic Genomics
The Institute for Genomic Research
9712 Medical Center Dr., Rockville, MD 20850
Tel: 301 838 0200
Fax: 301 838 0208
Email: hbe@igir.org
Clones are derived from the human BAC library RPCI-11. For BAC library availability, please contact Pieter de Jong (pieter@dejong.med.buffalo.edu). Clones may be purchased from BACPAC Resources (<http://bacpac.med.buffalo.edu/ordering>) or from Research Genet. cs (info@resgen.com). BAC end search page: http://www.tigr.org/tldb/hungen/bac_end_search.html.
Seq primer: 17
Class: BAC ends.

FEATURES
Location/Qualifiers
1..132
/organism="Homo sapiens"
/db_xref="GDB:7580458"
/db_xref="taxon:9606"
/clones="RPCI-11-210131"
/clone_lib="RPCI-11"
/sex="Male"
/cell_type="Lymphocytes"
/note="Vector: pBAC3.6; Site_1: EcoRI; Site_2: EcoRI;
RPCI11 Human Male BAC Library"
43 a 19 c 44 g 26 t

BASE COUNT
CPIGIN

Query Match 84.0%; Score 16.8; DB 12: Length 132;
Best Local Similarity 90.0%; Pred. No. 7e-02;
Matches 18; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

Oy 1 gctgatattctgtgggaaa 20
||||| ||||| |||||
Dt 4 GCTGATGTTCTGGTGAGAAA 23

RESULT 15
BF758769/c 154 bp mRNA linear EST 12-JAN-2001
DEFINITION MF0-CI0451-161100-019-f05 CI0451 Homo sapiens cDNA, mRNA sequence.
ACCESSION BF758769
VERSION BF758769.1 GI:12106669
KEYWORDS EST
SOURCE human.

ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 154)
Dias Neto E., Garcia Correa R., Verjovski-Almeida S., Briones M.R., Nagai M.A., da Silva W. Jr., Zago M.A., Bordin S., Costa F.F., Goldman G.H., Carvalho A.F., Matsukuma A., Baia G.S., Simpson D.H., Brunstein A., de Oliveira P.S., Bucher P., Jondeneel C.V., O'Hare M.J., Soares F., Brentani R.R., Reis L.F., de Souza S.J. and Simpson A.J.
Shotgun sequencing of the human transcriptome with ORF expressed sequence tags

TITLE
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 97 (7), 3491-3496 (2000)
MEDLINE 20202663
COMMENT Contact: Simpson A.J.G.
Laboratory of Cancer Genetics
Ludwig Institute for Cancer Research
Rua Prof. Antonio Prudente 109, 4 andar, 01509-010, Sao Paulo-SP, Brazil
Tel: +55-11-2704922
Fax: +55-11-2707901
Email: asimpson@ludwig.org.br

This sequence was derived from the FAPESP/LICP Human Cancer Genome Project. This entry can be seen in the following URL
(<http://www.ludwig.org.br/scripts/gethtml2.pl?i=MR0&t2=MR0-CI0451-161100-019-f05&t3=2000-11-16&t4=1>)
Seq primer: puc 18 forward

High quality sequence stop: 153.
Location/Qualifiers
1..154
/organism="Homo sapiens"
/db_xref="taxon:9606"
/clone_lib="CI0451"
/dev_stage="Adult"

/note="Organ: colon; Vector: puc18; Site_1: SmaI; Site_2: SmaI; A mini-library was made by cloning products derived from ORSTES PCR (U.S. Letters Patent application No. 196,716 - Ludwig Institute for Cancer Research) profiles into the pUC 18 vector. Reverse transcription of tissue mRNA and cDNA amplification were performed under low stringency conditions."
56 a 27 c 40 g 31 t

BASE COUNT
ORIGIN

Query Match 84.0%; Score 16.8; DB 10: Length 154;
Best Local Similarity 90.0%; Pred. No. 7.2e-02;
Matches 18; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

Oy 1 gctgatattctgtgggaaa 20
||||| ||||| |||||
Dt 118 GCTGATGTTCTGGTGAGAAA 99

Search completed: July 18, 2002, 04:22:41
Job time: 6515 sec

Thermotabilization and thermoactivation of thermostable enzymes by trehalose and its application for the synthesis of full length cDNA. Proc. Natl. Acad. Sci. U.S.A. 95 (2), 520-524 (1998)
 Itoh, M., Kitsuina, T., Akiyama, J., Shibata, K., Izawa, M., Kawai, J., Iomaru, Y., Carninci, P., Shibata, Y., Ozawa, Y., Muramatsu, M., Okazaki, Y., and Hayashizaki, Y.
 Automated filtration-based high-throughput plasmid preparation system. Genome Res. 9 (5), 463-470 (1999)
 Carninci, P. and Hayashizaki, Y.
 High-efficiency full-length cDNA cloning. Methods Enzymol. 303, 19-44 (1999)
 Please visit our web site (<http://genome.rtc.riken.go.jp>) for further details.

FEATURES

Location/Qualifiers
 1..248
 /organism="Mus musculus"
 /strain="C57BL/6J"
 /db_xref="taxon:10090"
 /clone="803046806"
 /clone_lib="RIKEN full-length enriched, 15 days embryo male testis"
 /sex="male"
 /tissue_type="testis"
 /dev_stage="15 days embryo"
 /lab_host="DH10B"
 /note="Site_1: Sall; Site_2: BamHI; cDNA library was prepared and sequenced in Mouse Genome Encyclopedia Project of Genome Exploration Research Group in Riken Genomic Sciences Center and Genome Science Laboratory in PIKEN, Division of Experimental Animal Research in Riken contributed to prepare mouse tissues. 1st strand cDNA was primed with a primer [5'
 GAGAGAGAGAGATCCAGAGCTCTTTTITTTTITVN 3']. cDNA was prepared by using trehalose thermo-activated reverse transcriptase and subsequently enriched for full-length by cap-trapper. cDNA went through one round of subtraction to Pot = 185.0 Second strand cDNA was prepared with the Primer adapter of sequence [5'
 GAGAGAGAGATCTCGATTAAATTAATTAATCCGCCGCCGCC 3']. cDNA was cloned into the XhoI and BamHI sites. Vector: a modified pBluescript KS(+) after bulk excision from Lambda FLC 1. Cloning sites, 5' end: Sall; 3' end: BamHI."
 32 a 55 C 50 g 75 t

BASE COUNT

ORIGIN
 Query Match 85.0%; Score 17; DB 9; Length 219;
 Best Local Similarity 100.0%; Pred. No. 6.1e+02;
 Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 C 2 cgaatattctgtggga 18
 T 11
 G 61 CIGAAATCTGCGGGA 77

RESULT

LOCUS B0047357 248 bp mRNA linear EST 25-JUN-2000
 DEFINITION B0047357 RIKEN full-length enriched, adult male medulla oblongata Mus musculus cDNA clone 6330597K03 3', mRNA sequence.
 ACCESSION B0047357
 VERSION B0047357.1 GI:8454533
 KEYWORDS EST.
 SOURCE house mouse.
 ORGANISM Mus musculus

Eukaryota: Metazoa; Chordata: Craniata: Vertebrata: Euteleostomi: Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
 1 (bases 1 to 248)
 Kono, H., Aizawa, K., Akahira, S., Akiyama, J., Arakawa, I., Carninci, P., Endo, I., Fukuda, S., Fukunishi, I., Hara, A., Hayashizaki, N., Hirozane, T., Hori, F., Ishii, Y., Ishikawa, J., Ishikawa, I., Itoh, M., Izawa, M., Kadota, K., Kagawa, I., Kai, C., Kawai, J., Kikuchi, N., Kiyosawa, H., Kojima, Y., Kondo, S., Koya, S., Kuribara, C., Kusakabe, M.

REFERENCE

AUTHORS Kono, H., Aizawa, K., Akahira, S., Akiyama, J., Arakawa, I., Carninci, P., Endo, I., Fukuda, S., Fukunishi, I., Hara, A., Hayashizaki, N., Hirozane, T., Hori, F., Ishii, Y., Ishikawa, J., Ishikawa, I., Itoh, M., Izawa, M., Kadota, K., Kagawa, I., Kai, C., Kawai, J., Kikuchi, N., Kiyosawa, H., Kojima, Y., Kondo, S., Koya, S., Kuribara, C., Kusakabe, M.

Matsuyama, T., Miki, R., Mizuno, Y., Nakamura, M., Oda, H., Okazaki, Y., Ono, I., Owa, C., Saito, H., Sakai, K., Sato, K., Shibata, K., Shibata, Y., Shimamoto, Y., Shinagawa, A., Shiraki, T., Sogabe, Y., Sugahara, Y., Suzuki, H., Suzuki, H., Tagawa, A., Takahashi, F., Tomimaga, N., Toya, I., Tsunoda, Y., Watahiki, A., Watanabe, S., Yamamura, T., Yamakaki, I., Yano, R., Yasunishi, A., Yokota, T., Yoshida, K., Yoshiki, A., Yoshino, M., Muramatsu, M. and Hayashizaki, Y.
 RIKEN Mouse ESs (Konno, H., et al.)
 Unpublished (2000)
 Contact: Yoshihide Hayashizaki
 Laboratory for Genome Exploration Research Group, RIKEN Genomic Sciences Center (GSC), Yokohama Institute
 The Institute of Physical and Chemical Research (RIKEN)
 7-22 Suehiro-cho, Tsurumi-ku, Yokohama, Kanagawa 230-0045, Japan
 Tel: 81-45-503-9222
 Fax: 81-45-503-9216
 Email: genome-res@qsc.riken.go.jp/
 URL: <http://genome.qsc.riken.go.jp/>
 Carninci, P., Nishiyama, Y., Westover, A., Itoh, M., Nagaoka, S., Sasaki, N., Okazaki, Y., Muramatsu, M. and Hayashizaki, Y.
 Thermotabilization and thermoactivation of thermostable enzymes by trehalose and its application for the synthesis of full length cDNA. Proc. Natl. Acad. Sci. U.S.A. 95 (2), 520-524 (1998)
 Itoh, M., Kitsuina, T., Akiyama, J., Shibata, K., Izawa, M., Kawai, J., Iomaru, Y., Carninci, P., Shibata, Y., Ozawa, Y., Muramatsu, M., Okazaki, Y. and Hayashizaki, Y.
 Automated filtration-based high-throughput plasmid preparation system. Genome Res. 9 (5), 463-470 (1999)
 Carninci, P. and Hayashizaki, Y.
 High-efficiency full-length cDNA cloning. Methods Enzymol. 303, 19-44 (1999)
 Please visit our web site (<http://genome.rtc.riken.go.jp>) for further details.

FEATURES

Location/Qualifiers
 1..248
 /organism="Mus musculus"
 /strain="C57BL/6J"
 /db_xref="taxon:10090"
 /clone="6330597K03"
 /clone_lib="RIKEN full-length enriched, adult male medulla oblongata"
 /sex="male"
 /tissue_type="medulla oblongata"
 /dev_stage="adult"
 /lab_host="DH10B"
 /note="Site_1: Sall; Site_2: BamHI; cDNA library was prepared and sequenced in Mouse Genome Encyclopedia Project of Genome Exploration Research Group in Riken Genomic Sciences Center and Genome Science Laboratory in RIKEN, Division of Experimental Animal Research in Riken contributed to prepare mouse tissues. 1st strand cDNA was primed with a primer [5'
 GAGAGAGAGATCCAGAGCTCTTTTITTTTITVN 3']. cDNA was prepared by using trehalose thermo-activated reverse transcriptase and subsequently enriched for full-length by cap-trapper. cDNA went through one round of normalization to Rot = 10.0 and subtraction to Rot = 100.0. Second strand cDNA was prepared with the primer adapter of sequence [5'
 GAGAGAGAGATCTCGATTAAATTAATTAATCCGCCGCCGCC 3']. cDNA was cloned into the XhoI and BamHI sites. Vector: a modified pBluescript KS(+) after bulk excision from Lambda FLC 1. Cloning sites, 5' end: Sall; 3' end: BamHI."
 50 a 53 C 64 g 81 t

BASE COUNT

ORIGIN
 Query Match 85.0%; Score 17; DB 9; Length 248;
 Best Local Similarity 100.0%; Pred. No. 6.3e+02;
 Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 C 2 cgaatattctgtggga 18
 T 11
 G 61 CIGAAATCTGCGGGA 77

Eukaryota: Metazoa: Chordata: Craniata: Vertebrata: Euteleostomi:
 Mammalia: Eutheria: Primates: Catarrhini: Hominoidea: Pan.
 Fujiyama A., Hattori M., Toyoda A., Taylor I.D., Yada I.,
 Totoki Y., Watanabe H. and Sakaki Y.
 BAC end sequences of Library RPCI-43
 Unpublished
 2 (bases 1 to 688)
 Fujiyama A., Hattori M., Toyoda A., Taylor I.D., Yada I.,
 Totoki Y., Watanabe H. and Sakaki Y.
 Direct Submission
 Submitted (02-AUG-2001) Asao Fujiyama, The Institute of Physical
 and Chemical Research (RIKEN), Genomic Sciences Center (GSC), Japan
 1-7-22 Suehiro-chou, Tsurumi-ku, Yokohama, Kanagawa 230-0045, Japan
 (E-mail: chimpanzee@sc.riken.go.jp, URL: http://hgp.gsc.riken.go.jp/
 Tel: 81-45-503-9111, Fax: 81-45-503-9170)
 Clones are derived from the chimpanzee BAC library RPCI-43. This BAC
 end was generated during the R&D process and may have higher chance
 of clone tracking errors.
 PRIMERS

Sequencing: I7

LIBRARY
 Vector : pBAC3.6
 R.Site 1 : EcoRI
 R.Site 2 : EcoRI
 Location/Qualifiers
 1..688

FEATURES

source
 /organism="Pan troglodytes"
 /db_xref="taxon:9598"
 /clone="RP43-054H23.I7"
 /sex="male"
 /cell_type="lymphocytes"
 /clone_lib="RPCI-43 Chimpanzee Male BAC Library"
 242 a 115 c 127 g 201 t 2 others

BASE COUNT

ORIGIN

Query Match 87.0% Score 17.4; DB 12; Length 688;
 Best Local Similarity 94.7%; Pred. No. 4.8e-02;
 Matches 18; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 2 ctgatattctgtgggaaa 20
 |||||
 Db 261 CTCATTCGCGGGAAA 279

RESULT 7

AG181575
 LOCUS AG181575 697 bp DNA linear GSS 09-JAN-2002
 DEFINITION Pan troglodytes DNA, clone: RP43-054H23.I7, genomic survey
 sequence.
 ACCESSION AG181575
 VERSION AG181575.1 GI:16711255
 KEYWORDS GSS: GSS (genome survey sequence).
 SOURCE Pan troglodytes male lymphocytes DNA, clone: RP43-054H23.I7.
 Male BAC Library clone: RP43-054H23.I7.
 ORGANISM Pan troglodytes

Eukaryota: Metazoa: Chordata: Craniata: Vertebrata: Euteleostomi:
 Mammalia: Eutheria: Primates: Catarrhini: Hominoidea: Pan.

Fujiyama A., Hattori M., Toyoda A., Taylor I.D., Yada I.,
 Totoki Y., Watanabe H. and Sakaki Y.
 BAC end sequences of Library RPCI-43
 Unpublished
 2 (bases 1 to 697)
 Fujiyama A., Hattori M., Toyoda A., Taylor I.D., Yada I.,
 Totoki Y., Watanabe H. and Sakaki Y.
 Direct Submission
 Submitted (02-AUG-2001) Asao Fujiyama, The Institute of Physical
 and Chemical Research (RIKEN), Genomic Sciences Center (GSC),
 1-7-22 Suehiro-chou, Tsurumi-ku, Yokohama, Kanagawa 230-0045, Japan
 (E-mail: chimpanzee@sc.riken.go.jp, URL: http://hgp.gsc.riken.go.jp/
 Tel: 81-45-503-9111, Fax: 81-45-503-9170)

Clones are derived from the chimpanzee BAC library RPCI-43. This BAC
 end was generated during the R&D process and may have higher chance
 of clone tracking errors.

PRIMERS

Sequencing: I7

LIBRARY
 Vector : pBAC3.6
 R.Site 1 : EcoRI
 R.Site 2 : EcoRI
 Location/Qualifiers
 1..697

FEATURES

source
 /organism="Pan troglodytes"
 /db_xref="taxon:9598"
 /clone="RP43-054H23.I7"
 /sex="male"
 /cell_type="lymphocytes"
 /clone_lib="RPCI-43 Chimpanzee Male BAC Library"
 252 a 113 c 131 g 197 t 4 others

BASE COUNT

ORIGIN

Query Match 87.0% Score 17.4; DB 12; Length 697;
 Best Local Similarity 94.7%; Pred. No. 4.8e-02;
 Matches 18; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 2 ctgatattctgtgggaaa 20
 |||||

Db 260 CTCATTCGCGGGAAA 278

RESULT 8

AV011849
 LOCUS AV011849 176 bp mRNA linear EST 25-AUG-1999
 DEFINITION AV011849 Mus musculus 18-day embryo C57BL/6J Mus musculus cDNA
 clone 1110033K13, mRNA sequence.

ACCESSION AV011849
 VERSION AV011849.1 GI:4788836
 KEYWORDS EST.
 SOURCE house mouse.

ORGANISM

Mus musculus
 Eukaryota: Metazoa: Chordata: Craniata: Vertebrata: Euteleostomi:
 Mammalia: Eutheria: Rodentia: Sciurognathi: Muridae: Murinae: Mus.

REFERENCE

1 (bases 1 to 176)
 Carninci, P., Shibata, K., Ozawa, Y., Konno, H., Itoh, M., Alizawa, K.,
 Akahira, S., Akiyama, J., Fukuda, S., Fukunishi, Y., Funayama, T., Hara
 A., Hayatsu, N., Hori, F., Ishikawa, T., Itoh, M., Izawa, M., Kawai, J.,
 Kikuchi, N., Kojima, Y., Matsuyama, T., Naitsuma, H., Oda, H., Owa, C.,
 Sato, K., Shibata, Y., Shigemoto, I., Shiraki, T., Sogabe, Y., Sugahara
 Y., Suzuki, H., Suzuki, H., Tateo, M., Tomaru, Y., Tomimaga, N.,
 Muramatsu, M., Yamamura, T., Yokota, T., Yoshino, M.,
 RIKEN Mouse ESTs

JOURNAL

COMMENT

Unpublished (1999)
 Contact: Chie Owa
 Genome Science Laboratory

RIKEN
 3-1-1 Koyadai, Tsukuba, Ibaraki 305-0074, Japan

Tel: 91-298-36-9145
 Fax: 81-298-36-9098

Email: genome-res@sc.riken.go.jp

Thermotabilization and thermostabilization of full length cDNA
 trehalose and its application for the synthesis of full length cDNA
 (Proc. Natl. Acad. Sci. U.S.A. 95(2):520-524 (1998))
 Transcriptional sequencing: A method for DNA sequencing using RNA
 polymerase (Proc. Natl. Acad. Sci. U.S.A. 95(7):3455-3460 (1998))
 please visit our web site (<http://genome.rtc.riken.go.jp>) for
 further details.

FEATURES

source

Location/Qualifiers
 1..176
 /organism="Mus musculus"
 /strain="C57BL/6J"
 /db_xref="taxon:10090"
 /clone="1110033K13"

/db_xref="taxon:9606"
 /clone="plate=643 Col=5 Row=E"
 /clone_lib="RPC1-11 Human Male BAC Library"
 /sex="male"
 /note="Vector: pBACE3.6; Site:1: EcoRI; Site:2: EcoRI;
 Male blood DNA was isolated from one randomly chosen donor
 and partially digested with a combination of EcoRI and
 EcoRI Methylase. Size selected DNA was cloned into the
 pBACE3.6 vector at EcoRI sites"
 BASE COUNT 149 a 136 c 105 g 138 t 5 others
 CPIGIN

Query Match 90.0%; Score 18; DB 12; Length 533;
 Best Local Similarity 100.0%; Pred. No. 2.4e-02;
 Matches 18; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 2 cttatattctgtggaaa 19
 |||||
 Db 518 CIGATATCTGGTGGAA 501

RESULT 2
 EM188182/c
 LOCUS 551 bp mRNA linear EST 11-DEC-2001
 DEFINITION sa185107.y1 Gm-cl074 Glycine max cDNA clone SOYBEAN CLONE ID:
 Gm-cl074-3350 5' similar to IR:Q9Z166 O9Z166 ENDC-1.3-1
 4-BETA-D-GLUCANASE. ; mRNA sequence.

ACCESSION EM188182
 VERSION EM188182.1 GI:17519140
 KEYWORDS EST.
 SOURCE soybean.

ORGANISM Glycine max
 Eukaryota; Viridiplantae; Streptophyta; Embryophyta; Tracheophyta;
 Spermatophyta; Magnoliophyta; eudicotyledons; core eudicots;
 Rosidae; eurosids I; Fabales; Fabaceae; Papilionoideae; Phaseoleae;
 Glycine.

REFERENCE 1 (bases 1 to 551)
 Shoemaker R., Keim P., Vodkin L., Erpelting J., Corryell V., Khanna
 A., Bolla B., Marra M., Hillier L., Kucaba I., Martin J., Beck C.,
 Willie I., Underwood K., Steptoe M., Theising B., Allen M., Bowers
 Y., Person B., Swaller T., Gibbons M., Pape D., Harvey N., Schurk
 R., Ritter E., Kohn S., Shin I., Jackson Y., Cardenas M., McCann
 R., Waterston R. and Wilson R.
 Public Soybean EST Project
 Unpublished (1999)
 Contact: Shoemaker R/Public Soybean EST Project
 Public Soybean EST Project
 Washington University School of Medicine
 4444 Forest Park Parkway, Box 8501, St. Louis, MO 63109, USA
 Tel: 314 285 1800
 Fax: 314 285 1810
 Email: est@watson.wustl.edu

This clone is available through: Resgen, Invitrogen Corp. 2130
 South Memorial Parkway Huntsville, AL 35801 For further information
 call: (800)-533-4363 or contact: confresgen.com web site:
 www.resgen.com

Seq primer: -40pp from Gbco
 High quality sequence stop: 430.
 Location/Qualifiers

FEATURES
 Source
 1..551
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 /db_xref="taxon:3847"
 /clone="SOYBEAN CLONE ID: Gm-cl074-3350"
 /clone_lib="Gm-cl074"
 /tissue_type="seedlings induced for HR (hypersensitive
 response)"
 /dev_stage="9-11 day old"
 /lab_host="DH10B"
 /note="Vector: pBluescript II SK-; Site:1: EcoRI; Site:2:
 XhoI; The cDNA library was constructed from mRNA isolated
 from 9-11 day old seedlings that were induced for HR
 (hypersensitive response) by vacuum infiltrating plant

tissue with *Pseudomonas syringae* pv. *glycinea* carrying the
 avrB gene (Genetics 141:1597-1604). Plant tissue (expanded
 unifoliate leaves) was collected at 2, 4, 8, 12, 24, 36,
 and 53 hrs after inoculation and their mRNA pooled equally
 for cDNA construction. The library was prepared using the
 Stratagene pBluescript II SK(+) library construction kit.
 Complementary DNA was synthesized from mRNA using a primer
 consisting of a poly(dT) sequence with an XhoI restriction
 site. EcoRI adaptors were ligated to the blunt-ended cDNA
 fragments followed by XhoI digestion. The cDNA insert is
 protected from XhoI digestion via methylation during first
 strand synthesis. The cDNA fragments were directionally
 cloned into the EcoRI-XhoI restriction site of the
 pBluescript vector. The ligated cDNA fragments were
 transformed into *E. coli* Electromax DH10B host cells. Plant
 care, inoculations, and library construction were
 performed by Steve Clough (Mila Vodkin lab, University of
 Illinois)."

BASE COUNT 148 a 110 c 126 g 167 t
 CPIGIN

Query Match 90.0%; Score 18; DB 10; Length 551;
 Best Local Similarity 100.0%; Pred. No. 2.4e-02;
 Matches 18; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 3 tcatattctgtggaaa 20
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 Db 536 TGATATCTGGTGGAA 519

RESULT 3
 RE913740
 LOCUS 729 bp mRNA linear EST 29-SEP-2000
 DEFINITION 501669205F1 NCI_CGAP_Maml Mus musculus cDNA clone IMAGE:3969121 5'
 mRNA sequence.

ACCESSION RE913740.1 GI:10411662
 VERSION RE913740
 KEYWORDS EST.
 SOURCE house mouse.

ORGANISM Mus musculus
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
 1 (bases 1 to 729)

REFERENCE NIH-MGC <http://mgi.nci.nih.gov/>
 National Institutes of Health, Mammalian Gene Collection (MGC)
 Unpublished (1999)

AUTHORS Contact: Robert Strausberg, Ph.D.
 Email: cgapbs-r@mail.nih.gov
 Tissue Procurement: Gilbert Smith, Ph.D.
 cDNA Library Preparation: Life Technologies, Inc.
 DNA Library Arrayed by: The I.M.A.G.E. Consortium (LINL)
 DNA Sequencing by: Incyte Genomics, Inc.

Clone distribution: MGC clone distribution information can be
 found through the I.M.A.G.E. Consortium/LINL at:
<http://image.llnl.gov>
 Plate: LLAM9146 row: j column: 02
 High quality sequence stop: 724.
 Location/Qualifiers

FEATURES
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 /organism="Mus musculus"
 /strain="FVB/N"
 /db_xref="taxon:10090"
 /clone="IMAGE:3969121"
 /clone_lib="NCI_CGAP_Maml"
 /tissue_type="tumor biopsy sample"
 /dev_stage="10 months, virgin"
 /lab_host="DH10B"
 /note="Organ: mammary; Vector: pCMV-SPORT6; Site:1: SalI;
 Site:2: NotI; Cloned unidirectionally. Primer: Oligo dT.
 Library constructed by Life Technologies. Investigator
 providing samples: Gilbert Smith, NIH"

BASE COUNT 152 a 182 c 236 g 159 t

Search completed: July 18, 2002, 04:56:38
Job time: 8267 sec

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: APPLICANT: Philippsen, Peter
: APPLICANT: Pohlmann, Rainer
: APPLICANT: Steiner, Sabine
: APPLICANT: Mohr, Christine
: APPLICANT: Wendland, Jurgen
: APPLICANT: Knechtle, Philipp
: APPLICANT: Rebschuing, Corinne
: TITLE OF INVENTION: GENOMIC DNA SEQUENCES OF ASHBYA GOSSEYII
: TITLE OF INVENTION: AND USES THEREOF
: NUMBER OF SEQUENCES: 1152
: CORRESPONDENCE ADDRESS:
: ADDRESSEE: No. 6239264artis Corporation
: STREET: 3054 Cornwallis Road
: CITY: Research Triangle Park
: STATE: No. 5239264th Carolina
: COUNTRY: USA
: ZIP: 27709
: COMPUTER READABLE FORM:
: MEDIUM TYPE: Floppy disk
: OPERATING SYSTEM: IBM PC compatible
: SOFTWARE: Patent In Release #1.0, Version #1.30
: CURRENT APPLICATION DATA:
: APPLICATION NUMBER: US/08/998,416
: FILING DATE: 24-DEC-1997
: CLASSIFICATION: 435
: PRIOR APPLICATION DATA:
: APPLICATION NUMBER: CH 0016/97
: FILING DATE: 31-DEC-1996
: ATTORNEY/AGENT INFORMATION:
: NAME: Weigs, J. Timothy
: REGISTRATION NUMBER: 38,241
: REFERENCE/DOCKET NUMBER: PF/5-30306/A/CGC1976
: TELECOMMUNICATION INFORMATION:
: TELEPHONE: 919-541-8587
: TELEFAX: 919-541-8689
: INFORMATION FOR SEQ ID NO: 900:
: SEQUENCE CHARACTERISTICS:
: LENGTH: 711 base pairs
: TYPE: nucleic acid
: STRANDEDNESS: single
: TOPOLOGY: linear
: MOLECULE TYPE: DNA (genomic)
: ORIGINAL SOURCE:
: ORGANISM: PAG1561UP
: US-08-998-416-900

Query Match 76.0%; Score 15.2; DB 4; Length 711;
Best Local Similarity 85.0%; Pred. No. 45;
Matches 17; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

Oy 1 gctgatattctggtaggaaa 20
Db 96 GTGACCTTCGTCGGGAAA 115

RESULT 11
US-08-772-440-33
: Sequence 33, Application US/08772440
: GENERAL INFORMATION:
: APPLICANT: Arizumi, Kiyoshi
: APPLICANT: Takashima, Akira
: TITLE OF INVENTION: UNIQUE DENDRITIC CELL-ASSOCIATED C-TYPE
: TITLE OF INVENTION: LECTINS, DECTIN-1 AND DECTIN-2; COMPOSITIONS AND USES
: TITLE OF INVENTION: THEREOF
: NUMBER OF SEQUENCES: 42
: CORRESPONDENCE ADDRESS:
: ADDRESSEE: Arnold, White & Durkee
: STREET: P.O. Box 4433
: CITY: Houston
: STATE: Texas

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: COUNTRY: USA
: ZIP: 77210
: COMPUTER READABLE FORM:
: MEDIUM TYPE: Floppy disk
: OPERATING SYSTEM: IBM PC compatible
: SOFTWARE: Patent In Release #1.0, Version #1.30
: CURRENT APPLICATION DATA:
: APPLICATION NUMBER: US/08/772,440
: FILING DATE: CONCURRENTLY HERewith
: CLASSIFICATION: 435
: ATTORNEY/AGENT INFORMATION:
: NAME: Parker, David L.
: REGISTRATION NUMBER: 32,165
: REFERENCE/DOCKET NUMBER: UTXD:493
: TELECOMMUNICATION INFORMATION:
: TELEPHONE: 512/418-3000
: TELEFAX: 512/474-7577
: INFORMATION FOR SEQ ID NO: 33:
: SEQUENCE CHARACTERISTICS:
: LENGTH: 10409 base pairs
: TYPE: nucleic acid
: STRANDEDNESS: single
: TOPOLOGY: linear
: FEATURE:
: NAME/KEY: modified_base
: LOCATION: 6510
: OTHER INFORMATION: /mod_base= OTHER
: OTHER INFORMATION: /note= "D = A or G or T"
: FEATURE:
: NAME/KEY: modified_base
: LOCATION: 3406..6470
: OTHER INFORMATION: /mod_base= OTHER
: OTHER INFORMATION: /note= "K = G or T"
: FEATURE:
: NAME/KEY: modified_base
: LOCATION: 3554..7896
: OTHER INFORMATION: /mod_base= OTHER
: OTHER INFORMATION: /note= "M = A or C"
: FEATURE:
: NAME/KEY: modified_base
: LOCATION: 3497..3607
: OTHER INFORMATION: /mod_base= OTHER
: OTHER INFORMATION: /note= "N = A or C or G or T"
: FEATURE:
: NAME/KEY: modified_base
: LOCATION: 3479..6422
: OTHER INFORMATION: /mod_base= OTHER
: OTHER INFORMATION: /note= "R = A or G"
: FEATURE:
: NAME/KEY: modified_base
: LOCATION: 3405..6871
: OTHER INFORMATION: /mod_base= OTHER
: OTHER INFORMATION: /note= "S = C or G"
: FEATURE:
: NAME/KEY: modified_base
: LOCATION: 3457..9998
: OTHER INFORMATION: /mod_base= OTHER
: OTHER INFORMATION: /note= "W = A or T"
: FEATURE:
: NAME/KEY: modified_base
: LOCATION: 3595..9999
: OTHER INFORMATION: /mod_base= OTHER
: OTHER INFORMATION: /note= "Y = C or T"
: US-08-772-440-33

Query Match 76.0%; Score 15.2; DB 3; Length 10409;
Best Local Similarity 85.0%; Pred. No. 68;
Matches 17; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

Oy 1 gctgatattctggtaggaaa 20
Db 96 GTGACCTTCGTCGGGAAA 115

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MOLECULE TYPE: DNA (genomic)
US-09-032-742-3

Query Match 82.0%; Score 16.4; DB 4; Length 2246;
Best Local Similarity 94.4%; Pred. No. 13;
Matches 17; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 gctgatattctgtgga 18
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Db 982 GCGATATGCTGGGGA 999

RESULT 5

US-09-032-742-21
Sequence 21, Application US/09032742
Patent No. 6255089

GENERAL INFORMATION:

APPLICANT: Teitler, Milt
APPLICANT: Herrick-Davis, Katharine
TITLE OF INVENTION: Constitutively Activated Serotonin
NUMBER OF SEQUENCES: 25
CORRESPONDENCE ADDRESS:
ADDRESSEE: Laurence Weinberger
STREET: 882 S. Matlack Street, Suite 103
CITY: West Chester
STATE: PA
COUNTRY: USA
ZIP: 19380-0053

COMPUTER READABLE FORM:
MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: PatentIn Release #1.0, Version #1.30
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/032,742
FILING DATE: 27-FEB-1998
CLASSIFICATION: 536

ATTORNEY/AGENT INFORMATION:
NAME: Weinberger, Laurence
REGISTRATION NUMBER: 27,965
REFERENCE/DOCKET NUMBER: 3086-4
TELECOMMUNICATION INFORMATION:
TELEPHONE: (610) 431-1703
TELEFAX: (610) 431-4181
INFORMATION FOR SEQ ID NO: 21:
SEQUENCE CHARACTERISTICS:
LENGTH: 2246 base pairs
TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: DNA (genomic)
US-09-032-742-21

Query Match 82.0%; Score 16.4; DB 4; Length 2246;
Best Local Similarity 94.4%; Pred. No. 13;
Matches 17; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 gctgatattctgtgga 18
|||||
Db 982 GCGATATGCTGGGGA 999

RESULT 6

US-09-032-742-22
Sequence 22, Application US/09032742
Patent No. 6255089

GENERAL INFORMATION:

APPLICANT: Teitler, Milt

APPLICANT: Herrick-Davis, Katharine
APPLICANT: Egan, Christina C.
TITLE OF INVENTION: Constitutively Activated Serotonin
NUMBER OF SEQUENCES: 25
CORRESPONDENCE ADDRESS:
ADDRESSEE: Laurence Weinberger
STREET: 882 S. Matlack Street, Suite 103
CITY: West Chester
STATE: PA
COUNTRY: USA
ZIP: 19380-0053

COMPUTER READABLE FORM:
MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: PatentIn Release #1.0, Version #1.30
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/032,742
FILING DATE: 27-FEB-1998
CLASSIFICATION: 536

ATTORNEY/AGENT INFORMATION:
NAME: Weinberger, Laurence
REGISTRATION NUMBER: 27,965
REFERENCE/DOCKET NUMBER: 3086-4
TELECOMMUNICATION INFORMATION:
TELEPHONE: (610) 431-1703
TELEFAX: (610) 431-4181
INFORMATION FOR SEQ ID NO: 22:
SEQUENCE CHARACTERISTICS:
LENGTH: 2246 base pairs
TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: DNA (genomic)
US-09-032-742-22

Query Match 82.0%; Score 16.4; DB 4; Length 2246;
Best Local Similarity 94.4%; Pred. No. 13;
Matches 17; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 gctgatattctgtgga 18
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Db 982 GCGATATGCTGGGGA 999

RESULT 7

US-09-032-742-24
Sequence 24, Application US/09032742
Patent No. 6255089

GENERAL INFORMATION:

APPLICANT: Teitler, Milt
APPLICANT: Herrick-Davis, Katharine
APPLICANT: Egan, Christina C.
TITLE OF INVENTION: Constitutively Activated Serotonin
NUMBER OF SEQUENCES: 25
CORRESPONDENCE ADDRESS:
ADDRESSEE: Laurence Weinberger
STREET: 882 S. Matlack Street, Suite 103
CITY: West Chester
STATE: PA
COUNTRY: USA
ZIP: 19380-0053

COMPUTER READABLE FORM:
MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: PatentIn Release #1.0, Version #1.30
CURRENT APPLICATION DATA:

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: STREET: 4 Embarcadero Center, Suite 3400
: CITY: San Francisco
: STATE: California
: COUNTRY: USA
: ZIP: 94111
: COMPUTER READABLE FORM:
: MEDIUM TYPE: Floppy disk
: COMPUTER: IBM PC compatible
: OPERATING SYSTEM: PC-DOS/MS-DOS
: SOFTWARE: PatentIn Release #1.0, Version #1.25
: CURRENT APPLICATION DATA:
: APPLICATION NUMBER: US/08/313,553
: FILING DATE:
: CLASSIFICATION: 435
: PRIOR APPLICATION DATA:
: APPLICATION NUMBER: US/08/038,652
: FILING DATE:
: ATTORNEY/AGENT INFORMATION:
: NAME: Dregger, Walter H.
: REGISTRATION NUMBER: 24,190
: REFERENCE/DOCKET NUMBER: A-57669/WHD
: TELECOMMUNICATION INFORMATION:
: TELEPHONE: (415) 781-1989
: TELEFAX: (415) 398-3249
: INFORMATION FOR SEQ ID NO: 10:
: SEQUENCE CHARACTERISTICS:
: LENGTH: 1848 base pairs
: TYPE: nucleic acid
: STRANDEDNESS: single
: TOPOLOGY: linear
: MOLECULE TYPE: cDNA
: FEATURE:
: NAME/KEY: misc_feature
: LOCATION: 1756..1758
: OTHER INFORMATION: /note= "Bacteriorhodopsin stop
: OTHER INFORMATION: codon."
: FEATURE:
: NAME/KEY: terminator
: LOCATION: 1756..1758
: OTHER INFORMATION: /note= "Helix I of rat serotonin:
: OTHER INFORMATION: receptor protein (Type IC)."
: FEATURE:
: NAME/KEY: misc_feature
: LOCATION: 517..591
: OTHER INFORMATION: /note= "Helix II of rat serotonin:
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: NAME/KEY: misc_feature
: LOCATION: 625..690
: OTHER INFORMATION: /note= "Helix III of rat serotonin:
: OTHER INFORMATION: receptor protein (Type IC)."
: FEATURE:
: NAME/KEY: misc_feature
: LOCATION: 736..807
: OTHER INFORMATION: /note= "Helix IV of rat serotonin:
: OTHER INFORMATION: receptor protein (Type IC)."
: FEATURE:
: NAME/KEY: misc_feature
: LOCATION: 828..933
: OTHER INFORMATION: /note= "Helix V of rat serotonin:
: OTHER INFORMATION: receptor protein (Type IC)."
: FEATURE:
: NAME/KEY: misc_feature
: LOCATION: 937..1059
: OTHER INFORMATION: /note= "Helix VI of rat serotonin:
: OTHER INFORMATION: receptor protein (Type IC)."
: FEATURE:
: NAME/KEY: misc_feature
: LOCATION: 1297..1362
: OTHER INFORMATION: /note= "Helix VII of rat serotonin:
: OTHER INFORMATION: receptor protein (Type IC)."
: FEATURE:
: NAME/KEY: misc_feature

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: LOCATION: 1411..1476
: OTHER INFORMATION: /note= "Helix VII of rat serotonin:
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: NAME/KEY: mutation
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: OTHER INFORMATION: /note= "G to A mutation removes
: OTHER INFORMATION: AluNI restriction site."
: FEATURE:
: NAME/KEY: misc_feature
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: OTHER INFORMATION: /note= "Codon encoding the
: OTHER INFORMATION: C-terminal amino acid of the rat serotonin
: OTHER INFORMATION: receptor protein (Type IC)."
: FEATURE:
: NAME/KEY: misc_signal
: LOCATION: 374
: OTHER INFORMATION: /note= "RNA start site."
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: NAME/KEY: CDS
: LOCATION: 376..1734
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: NAME/KEY: terminator
: LOCATION: 1735..1737
: OTHER INFORMATION: /note= "Serotonin stop codon."
: FEATURE:
: NAME/KEY: repeat_region
: LOCATION: 436..462
: OTHER INFORMATION: /note= "Sequence encoding
: OTHER INFORMATION: Patent No. 5641550
: OTHER INFORMATION: polyaspartic acid."
: FEATURE:
: NAME/KEY: mutation
: LOCATION: replace(1755, "")
: OTHER INFORMATION: /note= "C to T mutation removes
: OTHER INFORMATION: AluNI restriction site."
: US-08-313-553-10

Query Match 82.0%; Score 16.4; DB 1; Length 1848;
Best Local Similarity 94.4%; Pred. No. 13;
Matches 17: Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 gcgtatattctgtggga 18
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DB 549 GCTGATATGCTGGGGA 556

RESULT 3
US-08-767-993-10
: Sequence 10, Application US/08767993
: Patent No. 6010885
: GENERAL INFORMATION:
: APPLICANT: TURNER, George J.
: APPLICANT: BEILACH, Mary C.
: TITLE OF INVENTION: EXPRESSION OF HETEROLOGOUS POLYPEPTIDES
: TITLE OF INVENTION: IN HALOBACTERIA
: NUMBER OF SEQUENCES: 15
: CORRESPONDENCE ADDRESS:
: ADDRESSEE: Walter H. Dregger
: STREET: 4 Embarcadero Center, Suite 3400
: CITY: San Francisco
: STATE: California
: COUNTRY: USA
: ZIP: 94111
: COMPUTER READABLE FORM:
: MEDIUM TYPE: Floppy disk
: COMPUTER: IBM PC compatible
: OPERATING SYSTEM: PC-DOS/MS-DOS
: SOFTWARE: PatentIn Release #1.0, Version #1.25
: CURRENT APPLICATION DATA:
: APPLICATION NUMBER: US/08/767,993
: FILING DATE:

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DR P-PSDB; ABC24634.
 XX New isolated polynucleotide and encoded polypeptides, useful in
 PI diagnostics, forensics, gene mapping, identification of mutations
 PI responsible for genetic disorders or other traits and to assess
 PI biodiversity
 XX
 PS Claim 1: SEQ ID No 24625; 103pp: English.
 XX
 CC The invention relates to isolated polynucleotide (I) and
 CC polypeptide (II) sequences. (I) is useful as hybridisation probes,
 CC polymerase chain reaction (PCR) primers, oligomers, and for chromosome
 CC and gene mapping, and in recombinant production of (II). The
 CC polynucleotides are also used in diagnostics as expressed sequence tags
 CC for identifying expressed genes. (I) is useful in gene therapy techniques
 CC to restore normal activity of (II) or to treat disease states involving
 CC (II). (II) is useful for generating antibodies against it, detecting or
 CC quantitating a polypeptide in tissue, as molecular weight markers and as
 CC a food supplement. (II) and its binding partners are useful in medical
 CC imaging of sites expressing (II). (I) and (II) are useful for treating
 CC disorders involving aberrant protein expression or biological activity.
 CC The polypeptide and polynucleotide sequences have applications in
 CC diagnostics, forensics, gene mapping, identification of mutations
 CC responsible for genetic disorders or other traits to assess biodiversity
 CC and to produce other types of data and products dependent on DNA and
 CC amino acid sequences. AAS64197-AAS94564 represent novel human
 CC diagnostic coding sequences of the invention.
 CC Note: The sequence data for this patent did not appear in the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 2469 BP: 575 A: 568 C: 704 G: 521 T: 1 other:

Query Match 84.0%; Score 16.8; DB 23; Length 2459;
 Best Local Similarity 90.0%; Pred. No. 68;
 Matches 18; Conservative 0; Mismatches 2; Indels 0; Gaps 0;
 QY 1 gctgaattcttggtgggaaa 20
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 DB 121 gcggatattctggtgggaaa 140

RESULT 15
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 ID AAS88825 standard; cDNA; 2829 BP.
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 AC AAS88825;
 XX
 DT 13-FEB-2002 (first entry)
 XX
 DE DNA encoding novel human diagnostic protein #24629.
 XX
 KW Human; chromosome mapping; gene mapping; gene therapy; forensic;
 KW food supplement; medical imaging; diagnostic; genetic disorder; ss.
 XX Homo sapiens.
 OS
 XX WO200175067-A2.
 FN
 XX 11-OCI-2001.
 FD
 XX 30-MAR-2001: 2001WO-US09631.
 FF
 XX 31-MAR-2000: 2000US-0540217.
 FR 23-AUG-2000: 2000US-0549167.
 XX
 XX (HYSE-) HYSEQ INC.
 XX
 XX Drmanac RI, Liu C, Tang YI:
 XX WPI; 2001-639362/73.
 XX P-PSDB; ABC24638.
 DP

XX New isolated polynucleotide and encoded polypeptides, useful in
 PI diagnostics, forensics, gene mapping, identification of mutations
 PI responsible for genetic disorders or other traits and to assess
 PI biodiversity
 XX
 PS Claim 1: SEQ ID No 24629; 103pp: English.
 XX
 CC The invention relates to isolated polynucleotide (I) and
 CC polypeptide (II) sequences. (I) is useful as hybridisation probes,
 CC polymerase chain reaction (PCR) primers, oligomers, and for chromosome
 CC and gene mapping, and in recombinant production of (II). The
 CC polynucleotides are also used in diagnostics as expressed sequence tags
 CC for identifying expressed genes. (I) is useful in gene therapy techniques
 CC to restore normal activity of (II) or to treat disease states involving
 CC (II). (II) is useful for generating antibodies against it, detecting or
 CC quantitating a polypeptide in tissue, as molecular weight markers and as
 CC a food supplement. (II) and its binding partners are useful in medical
 CC imaging of sites expressing (II). (I) and (II) are useful for treating
 CC disorders involving aberrant protein expression or biological activity.
 CC The polypeptide and polynucleotide sequences have applications in
 CC diagnostics, forensics, gene mapping, identification of mutations
 CC responsible for genetic disorders or other traits to assess biodiversity
 CC and to produce other types of data and products dependent on DNA and
 CC amino acid sequences. AAS64197-AAS94564 represent novel human
 CC diagnostic coding sequences of the invention.
 CC Note: The sequence data for this patent did not appear in the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 2829 BP: 644 A: 741 C: 823 G: 619 T: 2 other:

Query Match 84.0%; Score 16.8; DB 23; Length 2829;
 Best Local Similarity 90.0%; Pred. No. 69;
 Matches 18; Conservative 0; Mismatches 2; Indels 0; Gaps 0;
 QY 1 gctgaattcttggtgggaaa 20
 II |||||
 DB 949 gcggatattctggtgggaaa 968

Search completed: July 18, 2002, 05:03:04
 Job time: 5238 sec

XX Drmanac RT, Liu C, Tang YT;
 XX WPI: 2001-639362/73;
 XX P-PSDB: ABG24633.
 XX New isolated polynucleotide and encoded polypeptides, useful in
 XX diagnostics, forensics, gene mapping, identification of mutations
 XX responsible for genetic disorders or other traits and to assess
 XX biodiversity -
 XX Claim 1: SEQ ID No 24624; 103pp; English.
 XX The invention relates to isolated polynucleotide (I) and
 XX polypeptide (II) sequences. (I) is useful as hybridisation probes,
 XX polymerase chain reaction (PCR) primers, oligomers, and for chromosome
 XX and gene mapping, and in recombinant production of (II). The
 XX polynucleotides are also used in diagnostics as expressed sequence tags
 XX for identifying expressed genes. (I) is useful in gene therapy techniques
 XX to restore normal activity of (II) or to treat disease states involving
 XX (II). (II) is useful for generating antibodies against it, detecting or
 XX quantitating a polypeptide in tissue, as molecular weight markers and as
 XX a food supplement. (II) and its binding partners are useful in medical
 XX imaging of sites expressing (II). (I) and (II) are useful for treating
 XX disorders involving aberrant protein expression or biological activity.
 XX The polypeptide and polynucleotide sequences have applications in
 XX diagnostics, forensics, gene mapping, identification of mutations
 XX responsible for genetic disorders or other traits to assess biodiversity
 XX and to produce other types of data and products dependent on DNA and
 XX amino acid sequences. AAS64197-AAS94564 represent novel human
 XX diagnostic coding sequences of the invention.
 XX Note: The sequence data for this patent did not appear in the printed
 XX specification, but was obtained in electronic format directly from WIPO
 XX at ftp.wipo.int/pub/published_pct_sequences.
 XX Sequence 486 BP: 92 A; 117 C; 161 G; 116 T; 0 other;

Query Match 84.0%; Score 16.8; DB 23; Length 486;
 Best Local Similarity 90.0%; Pred. No. 55;
 Matches 18; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

Oy 1 gctgatatctctgtgggaaa 20
 || |||||
 Db 184 gcggatatctctgtgggaaa 203

RESULT 11
 AAS88827
 ID AAS88827 standard: cDNA: 2347 BP.
 AC AAS88827;
 XX 13-FEB-2002 (first entry)
 DE DNA encoding novel human diagnostic protein #24631.
 XX Human: chromosome mapping; gene mapping; gene therapy; forensic;
 XX food supplement; medical imaging; diagnostic; genetic disorder: ss.
 XX Homo sapiens.
 CS WO200175067-A2.
 FN 11-OCT-2001.
 XX 30-MAR-2001: 2001WO-US08631.
 XX 31-MAR-2000: 2000US-0540217.
 XX 23-AUG-2000: 2000US-0649167.
 XX (HYSE-) HYSEQ INC.
 XX Drmanac RT, Liu C, Tang YT;

PI Drmanac RT, Liu C, Tang YT;
 XX WPI: 2001-639362/73;
 XX P-PSDB: ABG24540.
 XX New isolated polynucleotide and encoded polypeptides, useful in
 XX diagnostics, forensics, gene mapping, identification of mutations
 XX responsible for genetic disorders or other traits and to assess
 XX biodiversity -
 XX Claim 1: SEQ ID No 24631; 103pp; English.
 XX The invention relates to isolated polynucleotide (I) and
 XX polypeptide (II) sequences. (I) is useful as hybridisation probes,
 XX polymerase chain reaction (PCR) primers, oligomers, and for chromosome
 XX and gene mapping, and in recombinant production of (II). The
 XX polynucleotides are also used in diagnostics as expressed sequence tags
 XX for identifying expressed genes. (I) is useful in gene therapy techniques
 XX to restore normal activity of (II) or to treat disease states involving
 XX (II). (II) is useful for generating antibodies against it, detecting or
 XX quantitating a polypeptide in tissue, as molecular weight markers and as
 XX a food supplement. (II) and its binding partners are useful in medical
 XX imaging of sites expressing (II). (I) and (II) are useful for treating
 XX disorders involving aberrant protein expression or biological activity.
 XX The polypeptide and polynucleotide sequences have applications in
 XX diagnostics, forensics, gene mapping, identification of mutations
 XX responsible for genetic disorders or other traits to assess biodiversity
 XX and to produce other types of data and products dependent on DNA and
 XX amino acid sequences. AAS64197-AAS94564 represent novel human
 XX diagnostic coding sequences of the invention.
 XX Note: The sequence data for this patent did not appear in the printed
 XX specification, but was obtained in electronic format directly from WIPO
 XX at ftp.wipo.int/pub/published_pct_sequences.
 XX Sequence 2347 BP: 551 A; 500 C; 697 G; 499 T; 0 other;

Query Match 84.0%; Score 16.8; DB 23; Length 2347;
 Best Local Similarity 90.0%; Pred. No. 68;
 Matches 18; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

Oy 1 gctgatatctctgtgggaaa 20
 || |||||
 Db 1172 gcggatatctctgtgggaaa 1191

RESULT 12
 AAS88575/c
 ID AAS88575 standard: cDNA: 2370 BP.
 AC AAS88575;
 XX 13-FEB-2002 (first entry)
 DE DNA encoding novel human diagnostic protein #24379.
 XX Human: chromosome mapping; gene mapping; gene therapy; forensic;
 XX food supplement; medical imaging; diagnostic; genetic disorder: ss.
 XX Homo sapiens.
 CS WO200175067-A2.
 FN 11-OCT-2001.
 XX 30-MAR-2001: 2001WO-US08631.
 XX 31-MAR-2000: 2000US-0540217.
 XX 23-AUG-2000: 2000US-0649167.
 XX (HYSE-) HYSEQ INC.
 XX Drmanac RT, Liu C, Tang YT;

RESULT 6
AAAF27670
ID AAF27670 standard; DNA: 20 BP.
XX AC
XX AAF27670;
DI 02-APR-2001 (first entry)
XX DE
XX DE Primer #3.
XX IL-1; interleukin: inflammation; infection: ss.
XX Unidentified.
XX OS
XX WO200100880-A2.
XX 04-JAN-2001.
XX 30-JUN-2000: 2000WO-US18318.
XX 30-JUN-1999: 99US-0345217.
XX (INTE-) INTERLEUKIN GENETICS INC.
XX Duff GW, Cox A, Camp NJ, Di Giovine FS;
XX WPI: 2001-102593/11.
XX Determining whether a subject has or is predisposed to disease
PI associated with IL-1 polymorphism involves determining presence of
PI marker or allele comprising IL-1 inflammatory haplotype.
XX Disclosure: Page 23; 84pp; English.

XX The present invention relates to a new method for determining whether
CC a subject has or is predisposed to developing a disease or condition
CC that is associated with an IL (interleukin)-1 inflammatory haplotype.
CC comprises detecting at least one allele of the haplotype, where the
CC presence of the allele indicates that the subject is predisposed to
CC the development or has the disease or condition.
CC The method is useful for determining whether a subject has or is
CC predisposed to inflammatory disease, a degenerative disease, an
CC immunological disorder, an infectious disease, trauma induced disease,
CC or cancer. The above conditions associated with an IL-1 inflammatory
CC haplotype can be treated or prevented by administering a therapeutic
CC that compensates for a causative mutation that is in linkage
CC disequilibrium with at least one IL-1 polymorphism.
XX Sequence 20 BP: 5 A; 2 C; 7 G; 6 T; 0 other:

Query Match 100.0%; Score 20; DB 22; Length 20;
Best Local Similarity 100.0%; Pred. No. 0.89;
Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 gctgatattctgtgggaaa 20
|||||
DB 1 gctgatattctgtgggaaa 20

RESULT 7
AAC91438
ID AAC91438 standard; DNA: 20 BP.
XX AC
XX AAC91438;
DI 20-MAR-2001 (first entry)
XX Human IL-1A polymorphic locus AFM087xal 5' PCR primer.
XX Human: IL-1A; interleukin-lalpha; IL-1B; interleukin-lbeta; IL-1FN;
KW interleukin-1 receptor antagonist; vasotropic; antiinflammatory;
KW hypotensive; anticoagulant; antilipemic; arterial restenosis:

restenosis associated allele; RAA; occlusive cardiovascular disorder;
restenosis detection; PCR primer: ss.

XX Homo sapiens.
XX WO200071753-A2.
XX 30-NOV-2000.
XX 24-MAY-2000: 2000WO-US14299.
XX 24-MAY-1999: 99US-0317674.
XX 01-NOV-1999: 99US-0431352.
XX (INTE-) INTERLEUKIN GENETICS INC.
XX Kornman KS, Duff GW, Crossman DC, Francis SE, Stephenson K;
XX WPI: 2001-025173/03.

XX Diagnosing or determining susceptibility to developing restenosis
PI involves detecting restenosis associated allele in a nucleic acid
PI sample.

XX Disclosure: Page 41; 129pp; English.

XX The present sequence is given in a specification relating to a method for
CC determining whether a subject has or is predisposed to developing an
CC arterial restenosis. The method comprises detecting a restenosis
CC associated allele (RAA) in a nucleic acid sample from the subject, where
CC detection of the RAA indicates that the subject has or is predisposed to
CC the development of a restenosis. The restenosis associated allele
CC pattern permits the diagnosis of occlusive cardiovascular disorder. The
CC diagnosis allows the most suitable treatment methods for restenosis to be
CC used e.g. selecting therapies for initial vascular stenosis most likely
CC to avoid subsequent stenoses. The detection methods identify restenosis
CC therapeutics, agonists and antagonists, (proteins, peptides,
CC peptidomimetics, small molecules or nucleic acids, e.g. anti-sense,
CC ribozyme and triplex nucleic acids) which are used to treat restenosis.
XX Sequence 20 BP: 5 A; 2 C; 7 G; 6 T; 0 other:

Query Match 100.0%; Score 20; DB 22; Length 20;
Best Local Similarity 100.0%; Pred. No. 0.89;
Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 gctgatattctgtgggaaa 20
|||||
DB 1 gctgatattctgtgggaaa 20

RESULT 8
AAC89183
ID AAC89183 standard; DNA: 20 BP.

XX AC
XX AAC89183;
DI 08-MAR-2001 (first entry)

XX Human microsatellite marker AFM087xal PCR primer #1.
XX Human: PCR primer; cardiant; vasotropic; polymorphic; chromosome 2q13;
KW interleukin-1 gene cluster; IL-1; cardiovascular disorder;
KW fragile plaque disorder; occlusive disorder; in-stent restenosis; ss.

XX Homo sapiens.
XX WO200072015-A2.

XX 30-NOV-2000.

XX 26-MAY-2000: 2000WO-US14775.

XX Claim 9; Page 8; 2lpp; English.

XX PCR primers AA228417-228418 are used to amplify the microsatellite markers associated with the allele situated on chromosome 2, containing the D2S121 locus. The D2S121 microsatellite markers are contained in the region of chromosome 2 containing the IL2 (interleukin 2) cluster of genes. The invention relates to a method for diagnosing asthma or a predisposition to asthma. The products of PCR primers AA228409-228418 are used to detect any alleles that may be connected with asthma. The D2S121*3 allele (PCR primers AA228409-228410 are used to amplify the associated microsatellite markers) is used in the claimed methods to identify children at risk of developing asthma by examination immediately after birth, potentially allowing the disease to be prevented. The methods may also allow a prognosis of the severity of a condition and responses to particular treatments.

XX Sequence 20 BP; 5 A; 2 C; 7 G; 6 T; 0 other;

Query Match 100.0%; Score 20; DB 20; Length 20;
Best Local Similarity 100.0%; Pred. No. 0.89;
Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 gctgattctgtgtggaaa 20
|||||

DB 1 gctgattctgtgtggaaa 20

RESULT 2

AA63773
ID AA63773 standard; DNA: 20 BP.

XX AC AA63773;

XX 08-FEB-2001 (first entry)

XX Human IL-1 gene 5' PCR primer.

XX Human; IL-1; interleukin-1; cytokine; systemic inflammatory response; sepsis; immunosuppressive; dermatological; antimicrobial; antiarthritic; IL-1 receptor antagonist; tumour necrosis factor alpha antagonist; interstitial lung disease; interstitial pneumonia; pulmonary fibrosis; rheumatoid arthritis; systemic lupus erythematosus; Sjogren's syndrome; systemic sclerosis; dermatomyositis; PCR primer; chromosome 2; ss.

XX Homo sapiens.

XX W0200060117-A2.

XX 12-OCT-2000.

XX 31-MAR-2000; 2000WO-US08492.

XX 02-APR-1999; 99US-0286108.

XX (INTE-) INTERLEUKIN GENETICS INC.

XX Duff GW, Di Giovine FS, Whyte M.

XX WPI: 2000-656234/63.

XX Method for predicting the risk of interstitial lung disease, comprising detecting an interleukin-1 receptor antagonist allele and tumour necrosis alpha allele or an allele in linkage disequilibrium with either of these alleles.

XX Claim 5; Page 40; 102pp; English.

XX The present sequence is provided in a specification relating to a method for determining whether a subject has or is predisposed to develop an interstitial lung disease. The method involves detecting an interleukin-1 receptor antagonist (IL-1RN) (-2018) allele 2, a tumour necrosis alpha

CC (INF-Ay³³⁰⁸) allele 2, or an allele in linkage disequilibrium with either of these two alleles. The method may be used to determine whether a subject has or is predisposed to develop an interstitial pneumonia or a pulmonary fibrosis and other disorders such as rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, systemic sclerosis, dermatomyositis. The method is also used for identifying molecules which can be used as therapeutics for treating interstitial lung disease.

XX Sequence 20 BP; 5 A; 2 C; 7 G; 5 T; 0 other;

Query Match 100.0%; Score 20; DB 21; Length 20;
Best Local Similarity 100.0%; Pred. No. 0.89;
Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 gctgattctgtgtggaaa 20
|||||

DB 1 gctgattctgtgtggaaa 20

RESULT 3

AA61927
ID AA61927 standard; DNA: 20 BP.

XX AC AA61927;

XX 20-NOV-2000 (first entry)

XX Human IL-1 gene cluster AFM087xal marker PCR primer, SEQ ID NO:13.

XX Human; IL-1 gene cluster; interleukin-1; chromosome 2q13-14; proinflammatory; cytokine; systemic inflammatory response; sepsis; dysregulation; pattern 2 allele; genotyping; centromere distal; polymorphic microsatellite anchor marker; AFM087xal; PCR primer; ss.

XX Homo sapiens.

XX W02000037679-A2.

XX 29-JUN-2000.

XX 01-NOV-1999; 99WO-US25633.

XX 30-OCT-1998; 98US-0183850.

XX (INTE-) INTERLEUKIN GENETICS INC.

XX Di Giovine FS, Duff GW.

XX WPI: 2000-442691/38.

XX Determining susceptibility to developing sepsis for preventing or treating sepsis, involves detecting an allele of interleukin-1 genetic pattern that leads to dysregulated inflammatory response.

XX Disclosure: Page 35; 66pp; English.

XX The invention relates to methods of determining an individual's susceptibility to developing and/or rapidly progressing into sepsis via genotyping of a member of the IL-1 (interleukin-1) gene cluster. The method comprises obtaining an IL-1 gene cluster nucleic acid from an individual and determining whether that individual's DNA contains at least one allele of an IL-1 genetic pattern that leads to a dysregulated inflammatory response. The presence of a pattern 2 allele or a marker in linkage disequilibrium with a pattern 2 allele in the sample, indicates that the patient has an increased susceptibility to developing sepsis.

XX The IL-1 gene cluster comprises a region of 430 kb which is located on the long arm of chromosome 2 (2q13-14). It contains the IL-1A gene which encodes IL-1-alpha, the IL-1B gene which encodes IL-1-beta, and the IL-1RN gene which encodes the IL-1 receptor antagonist. IL-1 is a proinflammatory cytokine released by macrophages which can induce a systemic response to local injury or infection. It thus plays a key role in the development of sepsis, which can lead to intravascular

COMMENT

On May 20, 2001 this sequence version replaced gi:7321474.
All repeats were identified using RepeatMasker:
Smit, A.F.A. & Green, P. (1996-1997)
<http://ftp.genome.washington.edu/RM/RepeatMasker.html>

----- Genome Center
Center: Whitehead Institute/ MIT Center for Genome Research

Center code: WIBR
Web site: <http://www.seq.wi.mit.edu>
Contact: sequence_submissions@genome.wi.mit.edu
----- Project Information
Center project name: L1026
Center clone name: 463.D.17

----- Summary Statistics
Sequencing vector: M13; M7815; 58% of reads
Sequencing vector: Plasmid; L08752; 2% of reads
Sequencing vector: n/a; 40% of reads
Chemistry: Dye-Primer-amerisham; 32% of reads
Chemistry: Dye-terminator Big Dye; 68% of reads
Assembly program: Phrap; version 0.960731
Consensus quality: 194152 bases at least Q40
Consensus quality: 194980 bases at least Q30
Consensus quality: 195410 bases at least Q20
Insert size: 190000; agarose-1p
Insert size: 195548.

* NOTE: This is a 'working draft' sequence. It currently
* consists of 4 contigs. The true order of the pieces
* is not known and their order in this sequence record is
* arbitrary. Gaps between the contigs are represented as
* runs of N, but the exact sizes of the gaps are unknown.
* This record will be updated with the finished sequence
* as soon as it is available and the accession number will
* be preserved.

* 1 1103: contig of 1103 bp in length
* 1104 1203: gap of 100 bp
* 1204 2349: contig of 1146 bp in length
* 2350 2449: gap of 100 bp
* 2450 3622: contig of 1173 bp in length
* 3623 3722: gap of 100 bp
* 3723 195848: contig of 192126 bp in length.

FEATURES

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/db_xref="taxon:9606"
/chromosome="18"
/map="18"
/clone_lib="RPC1-11 Human Male BAC"
misc_feature 1..1103
/note="assembly_fragment"
misc_feature 1204..2349
/note="assembly_fragment"
misc_feature 2450..3622
/note="assembly_fragment"
misc_feature 3723..195848
/note="assembly_fragment"
BASE COUNT 55839 a 41218 c 41843 g 56648 t 300 others
ORIGIN

Query Match 92.0%; Score 18.4; DB 2: Length 195848:

Best Local Similarity 95.0%; Pred. No. 39:
Matches 19: Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Cy 1 gctgatatcttgtggaaa 20
||||| ||||| ||||| |||||
Db 173628 GCIGAIGTCTGCTGGGAAA 173647

Search completed: July 18, 2002, 04:55:17
Job time: 8455 sec

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* 102578 112227: contig of 9550 bp in length
* 112228 112327: gap of 100 bp
* 112328 122049: contig of 9722 bp in length
* 122050 122149: gap of 100 bp
* 122150 126555: contig of 4506 bp in length
* 126556 126755: gap of 100 bp
* 126756 132018: contig of 5263 bp in length
* 132019 132118: gap of 100 bp
* 132119 135969: contig of 4851 bp in length
* 135970 137069: gap of 100 bp
* 137070 141509: contig of 4440 bp in length
* 141510 141609: gap of 100 bp
* 141610 147009: contig of 5400 bp in length
* 147010 147109: gap of 100 bp
* 147110 150145: contig of 3036 bp in length
* 150146 150245: gap of 100 bp
* 150246 153171: contig of 2926 bp in length
* 153172 153271: gap of 100 bp
* 153272 155871: contig of 2600 bp in length
* 155872 155971: gap of 100 bp
* 155972 158760: contig of 2789 bp in length
* 158761 158860: gap of 100 bp
* 158861 161580: contig of 2720 bp in length
* 161581 161680: gap of 100 bp
* 161681 163325: contig of 1645 bp in length
* 163326 163425: gap of 100 bp
* 163426 164786: contig of 1361 bp in length
* 164787 164886: gap of 100 bp
* 164887 166415: contig of 1529 bp in length
* 166416 166515: gap of 100 bp
* 166516 167540: contig of 1025 bp in length.

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FEATURES

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      /db_xref="taxon:9606"
      /chromosome="18"
      /map="18q12"
      /clone="RP11-749H17"
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      26781..43880
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      43981..61316
        /note="assembly_fragment"
      61417..77415
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      77516..90011
        /note="assembly_fragment"
      90112..102577
        /note="assembly_fragment"
      102678..112227
        /note="assembly_fragment"
      112328..122049
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      122150..126555
        /note="assembly_fragment clone_end:SP6 vector_side:left"
      126756..132018
        /note="assembly_fragment"
      132119..135969
        /note="assembly_fragment"
      137070..141509
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      141610..147009
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      147110..150145
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      150246..153171
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      153272..155871
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      158861..161580

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  163426..164786
    /note="assembly_fragment"
misc_feature
  164887..166415
    /note="assembly_fragment"
misc_feature
  166516..167540
    /note="assembly_fragment"
BASE COUNT 47707 a 35613 c 36261 g 45858 t 2101 others
ORIGIN

Query Match          92.0%  Score 18.4;  DB 2;  Length 167540;
Best Local Similarity 95.0%  Pred. No. 39;
Matches 19;  Conservative 0;  Mismatches 1;  Indels 0;  Gaps 0;

QY  1 actaatattctgtgagaaa 20
      ||||| ||||| ||||| |||||
BP 110467 GCTGATGCTCTGGTGGAAA 110486

RESULTS 13
AC009108
LOCUS       AC009108             170481 bp    DNA    linear    HTG 25-APR-2001
DEFINITION Homo sapiens chromosome 16 clone RP11-46309, WORKING DRAFT
SEQUENCE     4 ordered pieces.
ACCESSION   AC009108
VERSION     AC009108.9  GI:13786306
KEYWORDS    HTG: HTGS_PHASE2; HTGS_DRAFT: HTGS_ACTIVEFIN.
SOURCE      human.
ORGANISM    Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 170481)
AUTHORS    DOE Joint Genome Institute.
TITLE      Sequencing of Human Chromosome 16
JOURNAL     Unpublished
REFERENCE   2  (bases 1 to 170481)
AUTHORS    DOE Joint Genome Institute.
TITLE      Direct Submission
JOURNAL     Submitted (03-AUG-1999) Production Sequencing Facility, DOE Joint
            Genome Institute, 2800 Mitchell Drive, Walnut Creek, CA 94598, USA
            On Apr 25, 2001 this sequence version replaced gi:9964740.
COMMENT
-----Genome Center
Center: Joint Genome Institute
Center Code: JGI
Web site: http://www.jgi.doe.gov
-----
Project Information
Center Project Name: 584502
Center clone name: RPC1-11_46309
-----
Summary Statistics
Consensus quality: 167345 bases at least Q40
Consensus quality: 169423 bases at least Q30
Consensus quality: 169900 bases at least Q20
Estimated insert size: 181440; agarose-fp estimation
Estimated insert size: 170331; sum-of-contigs estimation
Quality coverage: 10.33 in Q20 bases; agarose-fp estimation
Quality coverage: 11.0 in Q20 bases; sum-of-contigs estimation.
* NOTE: This is a 'working draft' sequence. It currently
  * consists of 4 contigs. Gaps between the contigs
  * are represented as runs of N. The order of the pieces
  * is believed to be correct as given, however the sizes
  * of the gaps between them are based on estimates that have
  * been provided by the submitter.
  * This sequence will be replaced
  * by the finished sequence as soon as it is available and
  * the accession number will be preserved.
  * 1 24870: contig of 24870 bp in length
  * 24871 24970: gap of unknown length
  * 24971 37912: contig of 12942 bp in length

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* 47874 48569: contig of 696 bp in length
* 48570 48669: gap of 100 bp
* 48670 49329: contig of 660 bp in length
* 49330 49428: gap of 100 bp
* 49430 50112: contig of 683 bp in length
* 50113 50212: gap of 100 bp
* 50213 50836: contig of 624 bp in length
* 50837 50936: gap of 100 bp
* 50937 51616: contig of 680 bp in length
* 51617 51716: gap of 100 bp
* 51717 52397: contig of 681 bp in length
* 52398 52497: gap of 100 bp
* 52498 53185: contig of 688 bp in length
* 53186 53285: gap of 100 bp

Query Match          92.0%  Score 18.4; DB 2; Length 66227;
Best Local Similarity 95.0%  Pred. No. 41;
Matches 19: Conservative 0; Mismatches 1; Indels 0; Gaps 0;

OY 1 gctgatattctgtgggaaa 20
|||||
DB 40098 GCTTATATTCGTCGGAAA 40079

RESULT 11
AC079836
LOCUS       Homo sapiens chromosome 2 clone RP11-99K18, WORKING DRAFT SEQUENCE,
DEFINITION  25 unordered pieces.
ACCESSION   AC079836
VERSION     AC079836.3 GI:11323401
KEYWORDS    HIG; HIGS-PHASE1; HIGS-DRAFT.
SOURCE      human.
ORGANISM    Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
Waterston.R.H.
The sequence of Homo sapiens clone
Unpublished
Waterston.R.H.
2 (bases 1 to 153903)
Direct Submission
Submitted (12-SEP-2000) Genome Sequencing Center, Washington
University School of Medicine, 4444 Forest Park Parkway, St. Louis,
MO 63108, USA
On Nov 24, 2000 this sequence version replaced gi:10179389.

----- Genome Center -----
Center: Washington University Genome Sequencing Center
Center code: WUGSC
Web site: http://genome.wustl.edu/gsc/index.shtml
----- Project Information -----
Center project name: H_NH0099K18
----- Summary Statistics -----
Sequencing vector: Plasmid; 0%
Chemistry: Dye-primer; El: 94% of reads
Assembly program: Phrap; version 0.990319
Consensus quality: 140203 bases at least Q40
Consensus quality: 145183 bases at least Q30
Consensus quality: 147598 bases at least Q20
Insert size: 170000; agarose-ff
Insert size: 151503; sum-of-contigs
Quality coverage: 3.69 in Q20 bases; agarose-ff
Quality coverage: 4.24 in Q20 bases; sum-of-contigs
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* NOTE: This is a 'working draft' sequence. It currently
* consists of 25 contigs. The true order of the pieces
* is not known and their order in this sequence record is
* arbitrary. Gaps between the contigs are represented as
* runs of N, but the exact sizes of the gaps are unknown.

```

```

* This record will be updated with the finished sequence
* as soon as it is available and the accession number will
* be preserved.
*
* 1830: contig of 1830 bp in length
* 1831 1930: gap of unknown length
* 1931 3310: contig of 1380 bp in length
* 3311 5464: gap of unknown length
* 5465 5564: gap of unknown length
* 5565 7171: contig of 1607 bp in length
* 7172 7271: gap of unknown length
* 7272 9874: contig of 2603 bp in length
* 9875 9974: gap of unknown length
* 9975 11983: contig of 2009 bp in length
* 11984 12083: gap of unknown length
* 12084 14275: contig of 2192 bp in length
* 14276 14375: gap of unknown length
* 14376 17628: contig of 3253 bp in length
* 17629 17728: gap of unknown length
* 17729 21724: contig of 3996 bp in length
* 21725 21824: gap of unknown length
* 21825 25332: contig of 3508 bp in length
* 25333 25432: gap of unknown length
* 25433 27118: contig of 2286 bp in length
* 27119 27818: gap of unknown length
* 27819 30797: contig of 2979 bp in length
* 30798 30897: gap of unknown length
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* 35001 35100: gap of unknown length
* 35101 40321: contig of 5221 bp in length
* 40322 40421: gap of unknown length
* 40422 45944: contig of 5523 bp in length
* 45945 46044: gap of unknown length
* 46045 51804: contig of 5760 bp in length
* 51805 51904: gap of unknown length
* 51905 58214: contig of 6310 bp in length
* 58215 58314: gap of unknown length
* 58315 65112: contig of 6798 bp in length
* 65113 65212: gap of unknown length
* 65213 74226: contig of 9014 bp in length
* 74227 74327: gap of unknown length
* 74328 82657: contig of 8331 bp in length
* 82658 91941: gap of unknown length
* 91942 92041: contig of 9184 bp in length
* 92042 102415: gap of unknown length
* 102416 102515: contig of 10374 bp in length
* 102516 115951: gap of unknown length
* 115952 116051: contig of 13436 bp in length
* 116052 131428: gap of unknown length
* 131429 131528: contig of 15377 bp in length
* 131529 153903: contig of 22375 bp in length.

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FEATURES
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             1..153903
               /organism="Homo sapiens"
               /db_xref="taxon:9606"
               /chromosome="2"
             1..1830
               /note="assembly_name:Contig12"
             1931..3310
               /note="assembly_name:Contig13"
             clone_end.T7
               vector_side:right"
             3411..5464
               /note="assembly_name:Contig14"
             5565..7171
               /note="assembly_name:Contig15"
             7272..9874
               /note="assembly_name:Contig16"
             9975..11983
               /note="assembly_name:Contig17"
             12084..14275
               /note="assembly_name:Contig18"

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Query Match 100.0%; Score 20; DB 2; Length 185276;
 Best Local Similarity 100.0%; Pred. No. 5.4;
 Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 gctgattatctggtggaaa 20
 |||||
 Db 22816 GCGATATCTGTTGGGAAA 22797

RESULT 9
 AL627261/c 147777 bp DNA linear HTG 19-DEC-2001
 LOCUS Danio rerio clone RP71-IN11, *** SEQUENCING IN PROGRESS ***, in
 DEFINITION unordered pieces.
 ACCESSION AL627261
 VERSION AL627261.4 GI:17974055
 KEYWORDS HTG; HTGS_PHASE1; HTGS_DRAFT; HTGS_FULLTOP.
 SOURCE zebrafish.
 ORGANISM Danio rerio
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Actinopterygii; Neopterygii; Teleostei; Euteleostei; Ostariophysi;
 Cypriniformes; Cyprinidae; Danio.
 REFERENCE 1 (sites)
 AUTHORS Burton, J.
 TITLE Direct Submission
 JOURNAL Submitted (18-DEC-2001) Wellcome Trust Sanger Institute, Hinxton,
 Cambridgeshire, CB10 1SA, UK. E-mail enquiries:
 humquerry@sanger.ac.uk Clone requests: clonerequest@sanger.ac.uk
 On Dec 20, 2001 this sequence version replaced gi:16508354.

----- Genome Center
 Center: Wellcome Trust Sanger Institute
 Center code: SC
 Web site: http://www.sanger.ac.uk
 Contact: humquerry@sanger.ac.uk
 ----- Project Information
 Center project name: bZIN11
 ----- Summary Statistics
 Assembly program: XGAP4; version 4.5
 Sequencing vector: plasmid; L08752; 100% of reads
 Chemistry: dye-terminator Big Dye; 100% of reads
 Consensus quality: 145782 bases at least Q40
 Consensus quality: 146187 bases at least Q30
 Consensus quality: 146573 bases at least Q20
 Insert size: 145977; sum-of-contigs
 Insert size: 133003; 18.5% error; agarose-fp
 Quality coverage: 9.18x in Q20 bases; sum-of-contigs Quality
 coverage: 10.24x in Q20 bases; agarose-fp

 * NOTE: This is a 'working draft' sequence.
 * This record will be updated with the finished sequence
 * as soon as it is available and the accession number will
 * be preserved.

FEATURES Location/Qualifiers
 source 1..147777
 /organism="Danio rerio"
 /db_xref="taxon:7955"
 /clone="RP71-IN11"
 /clone_lib="RPC1-71"
 misc_feature 1..11250
 /note="assembly fragment:01799
 fragment_chain:1
 clone_end:SP6
 vector_side:left"
 misc_feature 11351..28894
 /note="assembly fragment:02192
 fragment_chain:1"
 misc_feature 28985..31208
 /note="assembly fragment:02277
 fragment_chain:1"
 misc_feature 31309..44590
 /note="assembly fragment:01705"

fragment_chain:1"
 44691..50341
 /note="assembly fragment:02974
 fragment_chain:1"
 50442..77356
 /note="assembly fragment:02335
 fragment_chain:1"
 77457..85291
 /note="assembly fragment:03275
 fragment_chain:1"
 85392..109028
 /note="assembly fragment:01218
 fragment_chain:1"
 109129..147777
 /note="assembly fragment:01091
 fragment_chain:1
 clone_end:T7
 vector_side:right"
 BASE COUNT 45528 a 25772 c 26968 g 47709 t 800 others
 ORIGIN

Query Match 95.0%; Score 19; DB 2; Length 147777;
 Best Local Similarity 100.0%; Pred. No. 19;
 Matches 19; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 2 ctgattatctggtggaaa 20
 |||||
 Db 99420 CTGATATCTGTTGGGAAA 99402

RESULT 10
 AC026534/c 66227 bp DNA linear HTG 22-MAR-2000
 LOCUS Homo sapiens chromosome 17 clone RP11-362L21 map 17, LOW-PASS
 DEFINITION SEQUENCE SAMPLING.
 ACCESSION AC026534
 VERSION AC026534.1 GI:7283233
 KEYWORDS HTG; HTGS_PHASE0.
 SOURCE human.
 ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (bases 1 to 66227)
 AUTHORS Birren, B., Linton, L., Nusbaum, C. and Lander, E.
 TITLE Homo sapiens chromosome 17, clone RP11-362L21
 JOURNAL Unpublished
 REFERENCE 2 (bases 1 to 66227)
 AUTHORS Birren, B., Linton, L., Nusbaum, C., Lander, E., Abraham, H., Allen, N.,
 Anderson, S., Baldwin, J., Barna, N., Bastien, V., Bida, F.,
 Boguslavskiy, L., Bouckgalter, B., Brown, A., Burkett, G., Collins, S.,
 Compagno, A., Cooke, P., DeArrellano, K., Dewar, K., Diaz, J.S.,
 Dodge, S., Domino, M., Doyle, M., Ferreira, P., FitzHugh, W., Gage, D.,
 Galagan, J., Gardyna, S., Ginde, S., Goyette, M., Graham, L.,
 Grand-Pierre, N., Grant, G., Hacos, B., Heaford, A., Horton, L.,
 Howland, J.C., Iliev, I., Johnson, R., Jones, C., Kann, L., Karatas, A.,
 Klein, J., Lacombe, K., Lamazares, R., Landers, T., Lehoczy, J.,
 Levine, R., Lien, C., Liu, S., Locke, K., Macdonald, P., Marquis, N.,
 McCarthy, M., McEwan, P., McGurk, A., McKernan, K., McPheeters, R.,
 Meldrum, J., Menees, L., Mihova, T., Miranda, C., Mlenda, V., Morrow, J.,
 Murphy, T., Naylor, J., Norman, C.H., O'Connor, T., O'Donnell, P.,
 O'Neil, D., Oliver, T.M., Oliver, J., Peterson, K., Pierre, N.,
 Pisani, C., Pollara, V., Raymond, C., Riley, R., Rogov, P., Rothman, D.,
 Roy, A., Santos, R., Schauer, S., Severy, P., Spencer, B.,
 Stange-Thomann, N., Stojanovic, N., Subramanian, A., Talamas, J.,
 Tassaye, S., Theodore, J., Tirrell, A., Travers, M., Trigilio, J.,
 Vassiliou, H., Viel, R., Vo, A., Wilson, B., Wu, X., Wyman, D., Ye, W.J.,
 Young, G., Zainoun, J., Zimmer, A. and Zody, M.

Direct Submission
 TITLE
 JOURNAL Submitted (22-MAR-2000) Whitehead Institute/MIT Center for Genome
 Research, 320 Charles Street, Cambridge, MA 02141, USA
 COMMENT All repeats were identified using RepeatMasker:

```

* 49478 51118: contig of 2641 bp in length
* 52119 52218: gap of unknown length
* 52219 54750: contig of 2532 bp in length
* 54750 54851: gap of unknown length
* 54851 57506: contig of 2656 bp in length
* 57506 61230: contig of 3624 bp in length
* 61230 61331: gap of unknown length
* 61331 65854: contig of 4524 bp in length
* 65854 69521: contig of 3667 bp in length
* 69521 69622: gap of unknown length
* 69622 71798: contig of 2077 bp in length
* 71798 71899: gap of unknown length
* 71899 75809: contig of 3911 bp in length
* 75809 80189: contig of 4280 bp in length
* 80189 80289: gap of unknown length
* 80289 84557: contig of 4568 bp in length
* 84557 84858: gap of unknown length
* 84858 88525: contig of 3859 bp in length
* 88525 89227: gap of unknown length
* 89227 93727: contig of 4801 bp in length
* 93727 93828: gap of unknown length
* 93828 97928: contig of 4001 bp in length
* 97928 103704: contig of 5776 bp in length
* 103704 103804: gap of unknown length
* 103804 109139: contig of 5335 bp in length
* 109139 109140: gap of unknown length
* 109140 114126: contig of 4887 bp in length
* 114126 114227: gap of unknown length
* 114227 119186: contig of 4950 bp in length
* 119186 119286: gap of unknown length
* 119286 124397: contig of 5111 bp in length
* 124397 124498: gap of unknown length
* 124498 131793: contig of 7296 bp in length
* 131793 131893: gap of unknown length
* 131893 131994: gap of unknown length
* 131994 138594: contig of 6801 bp in length
* 138594 138794: gap of unknown length
* 138794 145465: contig of 6671 bp in length
* 145465 145465: Location/Qualifiers
  source          1..145465
                  /organism="Homo sapiens"
                  /db_xref="taxon:9606"
                  /chromosome="3"
                  /map="3p"
                  /clone="RP11-348L20"
  misc_feature    1..1322
                  /note="assembly_name:Contig11"
  misc_feature    1423..2860
                  /note="assembly_name:Contig12"
  misc_feature    2951..4011
                  /note="assembly_name:Contig13"
  misc_feature    4112..5286
                  /note="assembly_name:Contig18"
  misc_feature    5387..7432
                  /note="assembly_name:Contig20"
  misc_feature    7533..8990
                  /note="assembly_name:Contig22"
  misc_feature    9091..10431
                  /note="assembly_name:Contig23"
  misc_feature    10532..12239
                  /note="assembly_name:Contig24"
  misc_feature    12340..13782
                  /note="assembly_name:Contig26"
  misc_feature    13883..15005
                  /note="assembly_name:Contig29"
  misc_feature    15105..16276
                  /note="assembly_name:Contig30"
  misc_feature    16377..18085
                  /note="assembly_name:Contig31"
  misc_feature    18186..19757

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/note="assembly_name:Contig32"
19868..21770
/note="assembly_name:Contig34"
21871..24168
/note="assembly_name:Contig35"
24269..26094
/note="assembly_name:Contig36"
26195..29446
/note="assembly_name:Contig37"
29547..32263

Query Match      100.0%   Score 20;   DB 2;   Length 145465;
Best Local Similarity 100.0%; Pred. No. 5.5;
Matches 20: Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 gctatattctgtggaaa 20
    |||||
Db 47644 GCTGATATTCGGGGAAA 47663

RESULT 8
AC104553/C
LOCUS      AC104553      185276 bp      DNA      linear      HTG 21-JAN-2002
DEFINITION Homo sapiens chromosome 2 clone RP11-295D2, *** SEQUENCING IN
PROGRESS ***, 35 unordered pieces.
ACCESSION  AC104553
VERSION     AC104553.2 GI:18252751
KEYWORDS   HTG; HTGS_PHASE1.
SOURCE      human.
ORGANISM    Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE  1 (bases 1 to 185276)
AUTHORS   Waterston,R.H.
TITLE     The sequence of Homo sapiens clone
JOURNAL   Unpublished
REFERENCE  2 (bases 1 to 185276)
AUTHORS   Waterston,R.H.
TITLE     Direct Submission
JOURNAL   Submitted (18-DEC-2001) Genome Sequencing Center, Washington
            University School of Medicine, 4444 Forest Park Parkway, St. Louis,
            MO 63108, USA
COMMENT    On Jan 21, 2002 this sequence version replaced gi:17921251.

----- Genome Center -----
Center: Washington University Genome Sequencing Center
Center code: WUGSC
Web site: http://genome.wustl.edu/gsc/index.shtml
----- Project Information -----
Center project name: H.NH0295D02
----- Summary Statistics -----
Sequencing vector: M13; 6%
Chemistry: Dye-primer ET; 0% of reads
Chemistry: Dye-terminator Big Dye; 100% of reads
Assembly program: Phrap; version 0.990319
Consensus quality: 173270 bases at least Q40
Consensus quality: 175899 bases at least Q30
Consensus quality: 177849 bases at least Q20
-----
* NOTE: This is a 'working draft' sequence. It currently
* consists of 35 contigs. The true order of the pieces
* is not known and their order in this sequence record is
* arbitrary. Gaps between the contigs are represented as
* runs of N, but the exact sizes of the gaps are unknown.
* This record will be updated with the finished sequence
* as soon as it is available and the accession number will
* be preserved.
* 1 1390: contig of 1390 bp in length
* 1391 1490: gap of unknown length
* 1491 3004: contig of 1514 bp in length
* 3005 3104: gap of unknown length
* 3105 4782: contig of 1678 bp in length

```


NOTICE: This sequence may not represent the entire insert of this clone. It may be shorter because we only sequence overlapping clone sections once, or longer because we provide a small overlap between neighboring data submissions.

This sequence was finished as follows unless otherwise noted: all regions were double stranded, sequenced with an alternate chemistry, or covered by high quality data (i.e., phred quality >= 30); an attempt was made to resolve all sequencing problems, such as compressions and repeats; all regions were covered by sequence from more than one subclone; and the assembly was confirmed by restriction digest.

MAPPING INFORMATION:

Mapping information for this clone was provided by Dr. John P. McPherson, Department of Genetics, Washington University, St. Louis MO. For additional information about the map position of this sequence, see <http://genome.wustl.edu/gsc>

SOURCE INFORMATION:

The RPL11 human BAC library was made from the blood of one male donor, as described by Osoegawa, K., Woon, P.-Y., Zhao, B., Frengen, E., Tateo, M., Catanese, J. J., and de Jong, P. J. (1998) An improved approach for construction of bacterial artificial chromosome libraries. *Genomics* 51:1-8. The clone may be obtained either from Research Genetics, Inc. (<http://www.resgen.com>) or Pieter de Jong and coworkers at the Roswell Park Cancer Institute (<http://bacpac.med.buffalo.edu>)

VECTOR: pBACE3.6

NEIGHBORING SEQUENCE INFORMATION:

The clone sequenced to the left is AL078621, 2000 bp overlap.

Actual end is at base position 142432 of RPL1-432G15.

There is an unresolved region from 107145 to 107172. Single plasmid region exists between 107078 and 107171.

FEATURES

SOURCE

```
1. 142432
   /organism="Homo sapiens"
   /db_xref="taxon:9606"
   /chromosome="2"
   /map="2"
```

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repeat_region 250..545
               /clone="RPL1-432G15"
               /clone_lib="RPL1-11"
               /rpt_family="Alu"
repeat_region 816..867
               /rpt_family="L2"
repeat_region 1020..1313
               /rpt_family="Alu"
repeat_region 1433..1727
               /rpt_family="Alu"
misc_feature 1970..2530
               /note="similar to EST AN070632 (NID:9025630) xa04d07.x1"
misc_feature 2822..2958
               /note="similar to EST BG724168 (NID:q14003355)"
repeat_region 4028..4424
               /rpt_family="ERV1"
repeat_region 4751..4777
               /rpt_family="(L1)"
repeat_region 6521..6686
               /rpt_family="(L1)"
repeat_region 6587..6887
               /rpt_family="MaLR"
repeat_region 6888..7234
               /rpt_family="MaLR"
repeat_region 7235..7457
               /rpt_family="MaLR"
repeat_region 7458..7856
               /rpt_family="MaLR"
repeat_region 7917..8069
               /rpt_family="MaLR"
repeat_region 8070..8249
               /rpt_family="MaLR"
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repeat_region 8145..8254
               /rpt_family="L2"
repeat_region 8479..8561
               /rpt_family="MaLR"
misc_feature 8601..8682
               /note="similar to EST AA446035 (NID:92158700) zw66a03.r1"
repeat_region 8812..8835
               /rpt_family="(L1)"
repeat_region 9215..9272
               /rpt_family="L2"
misc_feature 9509..9797
               /note="similar to EST AW935189 (NID:98110595)"
repeat_region 9974..10063
               /rpt_family="MaLR"
repeat_region 10123..10214
               /rpt_family="MaLR"
repeat_region 10272..10430
               /rpt_family="MaLR"
repeat_region 11094..11309
               /rpt_family="MaLR"
repeat_region 11278..11411
               /rpt_family="MaLR"
repeat_region 12126..12334
               /rpt_family="L1"
repeat_region 12315..12623
               /rpt_family="Alu"
repeat_region 12595..12821
               /rpt_family="(GAAA)n"
repeat_region 12632..13076
               /rpt_family="L1"
repeat_region 15346..15375
               /rpt_family="AT-rich"
repeat_region 15358..15413
               /rpt_family="L1"
repeat_region 15414..15700
               /rpt_family="Alu"
repeat_region 15701..16452
               /rpt_family="L1"
repeat_region 15901..15966
               /rpt_family="(TA)n"
repeat_region 16455..17157
               /rpt_family="MER2_type"
repeat_region 17158..17448
               /rpt_family="Alu"
repeat_region 17449..17890
               /rpt_family="MER2_type"
repeat_region 17924..18004
               /rpt_family="L1"
repeat_region 18005..18306
               /rpt_family="Alu"
repeat_region 18282..18306
               /rpt_family="(A)n"
repeat_region 18307..18898
               /rpt_family="L1"
repeat_region 18904..19182
               /rpt_family="Alu"
misc_feature 19060..19156
               /note="similar to EST AA446035 (NID:92158700) zw66a03.r1"
repeat_region 19185..19390
               /rpt_family="Alu"
repeat_region 19358..19401
               /rpt_family="(TAAA)n"
repeat_region 19397..20088
               /rpt_family="L1"
repeat_region 20089..20494
               /rpt_family="MaLR"
repeat_region 20495..21768
               /rpt_family="L1"
repeat_region 21769..22140
               /rpt_family="MaLR"
repeat_region 22141..22239
               /rpt_family="L1"
repeat_region 22214..22249
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ORIGIN

Query Match 100.0%; Score 20; DB 6; Length 20;
 Best Local Similarity 100.0%; Pred. No. 9.1;
 Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 gctgaattctgtgggaaa 20
 |||
 Db 1 GCTGATATCTGGGGAAA 20

RESULT 2

AX052810 AX052810 20 bp DNA linear PAI 12-JAN-2001
 DEFINITION Sequence 20 from Patent WO0071753.
 ACCESSION AX052810
 VERSION AX052810.1 GI:12226967

KEYWORDS synthetic construct.
 SOURCE synthetic construct.
 ORGANISM artificial sequence.

REFERENCE 1 (bases 1 to 20)
 AUTHORS Kornman,K.S., Duff,G.W., Crossman,D.C., Francis,S.E. and
 Stephenson,K.

TITLE Diagnostics and therapeutics for restenosis
 JOURNAL Interleukin Genetics, Inc. (US)
 PATENT: WO 0071753-A 20 30-NOV-2000;

FEATURES
 1..20
 Location/Qualifiers
 /organism="synthetic construct"
 /db_xref="taxon:32630"

BASE COUNT 5 a 2 c 7 g 6 t
 ORIGIN /note="primer"

Query Match 100.0%; Score 20; DB 6; Length 20;
 Best Local Similarity 100.0%; Pred. No. 9.1;
 Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 gctgaattctgtgggaaa 20
 |||
 Db 1 GCTGATATCTGGGGAAA 20

RESULT 3

AX067270 AX067270 20 bp DNA linear PAI 24-JAN-2001
 DEFINITION Sequence 6 from Patent WO0100880.
 ACCESSION AX067270
 VERSION AX067270.1 GI:12544894

KEYWORDS synthetic construct.
 SOURCE synthetic construct.
 ORGANISM artificial sequence.

REFERENCE 1 (bases 1 to 20)
 AUTHORS Duff,G.W., Cox,A., Camp,N.J. and di Giovine,F.S.

TITLE Diagnostics and therapeutics for diseases associated with an il-1
 inflammatory haplotype
 JOURNAL Patent: WO 0100880-A 6 04-JAN-2001;
 Interleukin Genetics, Inc. (US)

FEATURES
 1..20
 Location/Qualifiers
 /organism="synthetic construct"
 /db_xref="taxon:32630"

BASE COUNT 5 a 2 c 7 g 5 t
 ORIGIN /note="primer"

Query Match 100.0%; Score 20; DB 6; Length 20;
 Best Local Similarity 100.0%; Pred. No. 9.1;

Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 gctgaattctgtgggaaa 20
 |||
 Db 1 GCTGATATCTGGGGAAA 20

RESULT 4

HS087XA1 HS087XA1 213 bp DNA linear PRI 28-NOV-1994
 DEFINITION H. sapiens (D2S121) DNA segment containing (CA) repeat; clone
 AFM087xa1; single read.

ACCESSION Z16545
 VERSION Z16545.1 GI:23080
 KEYWORDS CA repeat; dinucleotide repeat; GT repeat; microsatellite DNA;
 microsatellite marker; repeat polymorphism.

SOURCE human.
 ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 WEISSENBAACH, J.

REFERENCE 1 (bases 1 to 213)
 AUTHORS Direct Submission
 JOURNAL Submitted (05-OCT-1992) Genethon, B.P. 60, 91002 Evry Cedex France.

REFERENCE 2 (bases 1 to 213)
 AUTHORS E-mail: Jean.Weissenbach@genethon.fr
 WEISSENBAACH, J., GYAPAY, G., DIB, C., VIGNAL, A., MORISSETTE, J.,
 MILLASSEAU, P., VAYSSEIX, G. and LATHROP, M.

TITLE A second-generation linkage map of the human genome
 JOURNAL Nature 359 (6398), 794-801 (1992)
 MEDLINE 93063290

REFERENCE 3 (bases 1 to 213)
 AUTHORS Gyapay,G., Morissette,J., Vignal,A., Dib,C., Fizames,C.,
 Millasseau,P., Marc,S., Bernardi,G., Lathrop,M. and Weissenbach,J.

TITLE The 1993-94 Genethon human genetic linkage map
 JOURNAL Nat. Genet. 7 (2 Spec No), 246-339 (1994)
 MEDLINE 95004593

COMMENT Cloning vector is M13mpl8;
 full automatic.
 FEATURES Location/Qualifiers

1..213
 source
 /organism="Homo sapiens"
 /db_xref="taxon:9606"
 /chromosome="2"
 /cell_line="CEPH 134702"
 /clone_lib="genomic DNA"
 BASE COUNT 73 a 49 c 42 g 49 t
 ORIGIN

Query Match 100.0%; Score 20; DB 9; Length 213;
 Best Local Similarity 100.0%; Pred. No. 7.9;
 Matches 20; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 gctgaattctgtgggaaa 20
 |||
 Db 2 GCTGATATCTGGGGAAA 21

RESULT 5

AC069268 AC069268 125685 bp DNA linear HTG 23-MAY-2000
 DEFINITION Homo sapiens chromosome 3p clone RP11-348I20, WORKING DRAFT
 SEQUENCE, 31 unordered pieces.

ACCESSION AC069268
 VERSION AC069268.1 GI:8039671
 KEYWORDS HTG; HTGS_PHASE1; HTGS_DRAFT.

SOURCE human.
 ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (bases 1 to 125685)
 AUTHORS Wang,J., Hu,S., Dong,W., Wang,J., Zhang,Y., Zhang,H., Liu,B.,